```
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TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  AUG 15  CAOLD to be discontinued on December 31, 2008
 NEWS  3  OCT 07  EPFULL enhanced with full implementation of EPC2000
 NEWS  4  OCT 07  Multiple databases enhanced for more flexible patent
                  number searching
 NEWS  5  OCT 22  Current-awareness alert (SDI) setup and editing
                  enhanced
 NEWS  6  OCT 22  WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT
                  Applications
 NEWS  7  OCT 24  CHEMLIST enhanced with intermediate list of
                  pre-registered REACH substances
 NEWS  8  NOV 21  CAS patent coverage to include exemplified prophetic
                  substances identified in English-, French-, German-,
                  and Japanese-language basic patents from 2004-present
 NEWS  9  NOV 26  MARPAT enhanced with FSORT command
 NEWS 10  NOV 26  MEDLINE year-end processing temporarily halts
                  availability of new fully-indexed citations
 NEWS 11  NOV 26  CHEMSAFE now available on STN Easy
 NEWS 12  NOV 26  Two new SET commands increase convenience of STN
                  searching
 NEWS 13  DEC 01  ChemPort single article sales feature unavailable
 NEWS 14  DEC 12  GBFULL now offers single source for full-text
                  coverage of complete UK patent families
 NEWS 15  DEC 17  Fifty-one pharmaceutical ingredients added to PS

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:43:27 ON 31 DEC 2008

=> fil reg
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.63	0.63

FILE 'REGISTRY' ENTERED AT 11:45:03 ON 31 DEC 2008
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STRUCTURE FILE UPDATES: 30 DEC 2008 HIGHEST RN 1092172-37-6
DICTIONARY FILE UPDATES: 30 DEC 2008 HIGHEST RN 1092172-37-6

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=>
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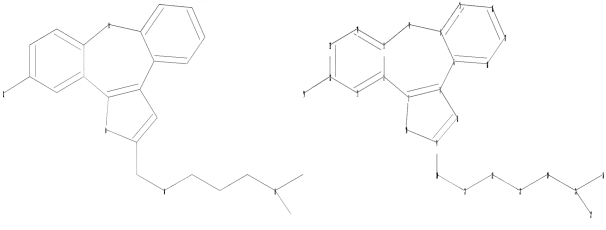


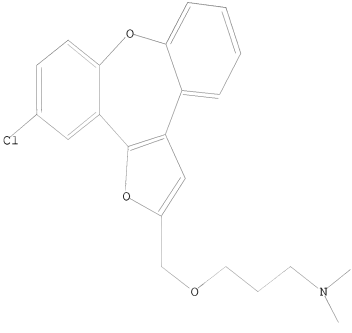
chain nodes :
19 20 21 22 23 24 25 26 27
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
chain bonds :
9-20 12-19 20-21 21-22 22-23 23-24 24-25 25-26 25-27
ring bonds :
1-2 1-7 1-10 2-3 2-11 3-4 3-14 4-5 5-6 5-15 6-7 6-18 7-8 8-9 9-10
11-12 12-13 13-14 15-16 16-17 17-18

exact/norm bonds :
1-2 1-7 1-10 3-4 4-5 6-7 7-8 8-9 9-10 20-21 21-22 24-25 25-26 25-27
exact bonds :
9-20 12-19 22-23 23-24
normalized bonds :
2-3 2-11 3-14 5-6 5-15 6-18 11-12 12-13 13-14 15-16 16-17 17-18

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> fil stng
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.47 1.10

FILE 'STNGUIDE' ENTERED AT 11:45:43 ON 31 DEC 2008
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Dec 19, 2008 (20081219/UP).

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=> fil reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.06       1.16

FILE 'REGISTRY' ENTERED AT 11:46:34 ON 31 DEC 2008
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STRUCTURE FILE UPDATES:   30 DEC 2008  HIGHEST RN 1092172-37-6
DICTIONARY FILE UPDATES:  30 DEC 2008  HIGHEST RN 1092172-37-6

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=>
Uploading C:\Program Files\STNEXP\Queries\10595935 generic.str
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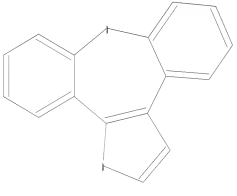

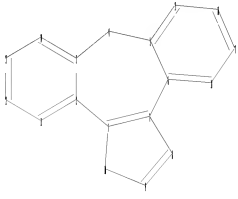

```
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18
ring bonds :
1-2  1-7  1-10  2-3  2-11  3-4  3-14  4-5  5-6  5-15  6-7  6-18  7-8  8-9  9-10
11-12  12-13  13-14  15-16  16-17  17-18
exact/norm bonds :
1-2  1-7  1-10  3-4  4-5  6-7  7-8  8-9  9-10
normalized bonds :
2-3  2-11  3-14  5-6  5-15  6-18  11-12  12-13  13-14  15-16  16-17  17-18


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom
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```
L2      STRUCTURE UPLOADED

=> s l2
SAMPLE SEARCH INITIATED 11:46:55 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    12106 TO ITERATE

 16.5% PROCESSED     2000 ITERATIONS                                 0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       235527 TO   248713
PROJECTED ANSWERS:               0 TO        0

L3            0 SEA SSS SAM L2

=> d l2
L2 HAS NO ANSWERS
L2              STR
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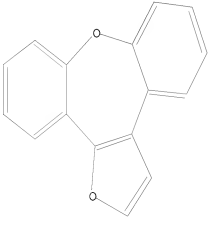

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Structure attributes must be viewed using STN Express query preparation.


=> s l2 sss ful;
FULL SEARCH INITIATED 11:47:21 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   241232 TO ITERATE

100.0% PROCESSED   241232 ITERATIONS                               12 ANSWERS
SEARCH TIME: 00.00.07

L4           12 SEA SSS FUL L2

=> s l1 sub=l3
ENTER SUBSET SEARCH SCOPE - SAMPLE, FULL, RANGE, OR (END):full
FULL SUBSET SEARCH INITIATED 11:47:39 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED -        0 TO ITERATE

100.0% PROCESSED        0 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01
```

```
L5            0 SEA SUB=L3 SSS FUL L1

=> s l1 sub=l2 sss ful
L2 MAY NOT BE USED HERE
The L-number must have been created by a search in this file.  To see
all L-numbers defined in this session, enter DISPLAY HISTORY at an
arrow prompt (=>).  For additional information on subset searching in
this file, enter HELP SUBSET.
ENTER SUBSET L# OR (END):l4
FULL SUBSET SEARCH INITIATED 11:48:15 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED -        1 TO ITERATE

100.0% PROCESSED        1 ITERATIONS                                 1 ANSWERS
SEARCH TIME: 00.00.01

L6            1 SEA SUB=L4 SSS FUL L1

=> fil cap
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   274.81     275.97

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FILE COVERS 1907 - 31 Dec 2008  VOL 150 ISS 1
FILE LAST UPDATED: 30 Dec 2008  (20081230/ED)

Caplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply.
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http://www.cas.org/legal/infopolicy.html

=> s l6
L7            2 L6

=> d l7 1-2 ibib abs hitstr

L7   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2005:471937  CAPLUS
DOCUMENT NUMBER:          143:1311
TITLE:                    Use of 1-oxadibenzo[e,h]azulenes for the manufacture
                          of pharmaceutical formulations for the treatment and
                          prevention of central nervous system diseases and
                          disorders
INVENTOR(S):              Mercep, Mladen; Mesic, Milan; Pesic, Dijana
```

PATENT ASSIGNEE(S): Pliva-Istrazivacki Institut D.O.O., Croatia
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005049010	A1	20050602	WO 2004-HR52	20041119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1684742	A1	20060802	EP 2004-798731	20041119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
JP 2007512306	T	20070517	JP 2006-540629	20041119
US 20070173493	A1	20070726	US 2006-595935	20060809

PRIORITY APPLN. INFO.: HR 2003-955 A 20031121
WO 2004-HR52 W 20041119

OTHER SOURCE(S): MARPAT 143:1311
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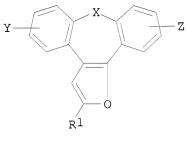


I

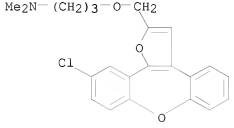
AB The present invention relates to the use of compds. from the group of 1-oxadibenzo[e,h]azulenes (I; X = CH2, heteroatom such as O, S, SO, SO2, amino; Y, Z = H, halo, alkyl, haloalkyl, hydroxy, alkoxy, amino, thiol, sulfonyl, carboxy, cyano, nitro, etc.; R1 = CHO, alkyl, amino, etc.) and of their pharmacol. acceptable salts and solvates for the manufacture of a pharmaceutical formulation for the treatment and prevention of diseases, damages and disorders of the central nervous system (CNS) caused by disorders of the neurochem. equilibrium of biogenic amines or other neurotransmitters, such as serotonin, norepinephrine and dopamine. Thus, an in vitro affinity of I compds. for binding to recombinant human 5-HT2A and 5-HT2C serotonin receptors expressed in CHO-K1 or COS-7 cells was determined using a radioligand. The radioligand binding was inhibited by the test compds. proportionally to the affinity of a certain compound for the receptor and to the concentration of the compound Compds. showing IC50 and Ki in

concns. lower than 1 μM were considered to be active. Compound 2-[(11-chloro-1,8-dioxadibenzo[e,h]azulen-2-yl-methoxy)ethyl]dimethylamine showed binding affinity to 5-HT2A and 5-HT2C receptors expressed as IC50 value less than 200 nM and Ki value less than 100 nM.

IT 628262-98-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oxadibenzoazulenes for treatment and prevention of CNS disorders by modulating biogenic amines or other neurotransmitters)

RN 628262-98-6 CAPLUS

CN 1-Propanamine, 3-[(11-chlorodibenzo[b,f]furo[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:931369 CAPLUS

DOCUMENT NUMBER: 140:5038

TITLE: Preparation of 1-oxa-dibenzoazulenes as inhibitors of tumor necrosis factor production and intermediates for the preparation thereof

INVENTOR(S): Mercep, Mladen; Mesic, Milan; Pesic, Dijana

PATENT ASSIGNEE(S): Pliva D.D., Croatia

SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097649	A2	20031127	WO 2003-HR24	20030520
WO 2003097649	A3	20040429		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2485214	A1	20031127	CA 2003-2485214	20030520
AU 2003232371	A1	20031202	AU 2003-232371	20030520
EP 1506204	A2	20050216	EP 2003-752867	20030520
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1665821	A	20050907	CN 2003-816107	20030520

CN 1315838	C	20070516			
JP 2005532327	T	20051027	JP 2004-505381		20030520
US 20050148577	A1	20050707	US 2004-995954		20041122
IN 2004CN02865	A	20060217	IN 2004-CN2865		20041216
US 20050209214	A1	20050922	US 2005-515678		20050603
HK 1081950	A1	20071123	HK 2006-102100		20060217
PRIORITY APPLN. INFO.:			HR 2002-441	A	20020521
			WO 2003-HR24	W	20030520

OTHER SOURCE(S): MARPAT 140:5038

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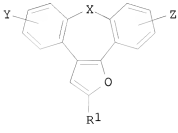


I

AB The title compds. [I; X = CH2, heteroatom such as O, S, SO, SO2, (un)protected NH; Y, Z = halo, alkyl, haloalkyl, alkoxy, etc.; R1 = (CH2)mQ1(CH2)nQ2NR2R3 (wherein R2, R3 = H, alkyl, aryl; or NR2R3 = heterocyclyl, heteroaryl; m, n = 0-3; Q1, Q2 = O, S, (un)substituted CH2, NH, CH:CH, C.tplbond.C)], which show antiinflammatory effects, especially the inhibition of tumor necrosis factor-α (TNF-α) production and the inhibition of interleukin-1 (IL-1) production as well as to analgesic action, were prepared Thus, reacting the alc. I [X = O; Y, Z = H; R1 = CH2OH] (preparation given) with 3-dimethylaminopropyl chloride hydrochloride afforded I [X = O; Y, Z = H; R1 = CH2O(CH2)3NMe2]. Preparation of intermediates I [X, Y, Z as above; R1 = Me, CHO, CH2OH] is also described.

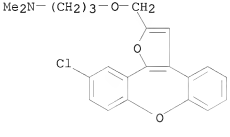
IT 628262-98-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 1-oxa-dibenzoazulenes as inhibitors of tumor necrosis factor production and intermediates for the preparation thereof)

RN 628262-98-6 CAPLUS

CN 1-Propanamine, 3-[(11-chlorodibenzo[b,f]furo[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> logoff

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ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    12.75     288.72

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -1.64      -1.64

STN INTERNATIONAL LOGOFF AT 11:49:59 ON 31 DEC 2008


Connecting via Winsock to STN



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LOGINID:SSPTAPEZ1617

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


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 NEWS  1           Web Page for STN Seminar Schedule - N. America
 NEWS  2  AUG 15   CAOLD to be discontinued on December 31, 2008
 NEWS  3  OCT 07   EPFULL enhanced with full implementation of EPC2000
 NEWS  4  OCT 07   Multiple databases enhanced for more flexible patent
                   number searching
 NEWS  5  OCT 22   Current-awareness alert (SDI) setup and editing
                   enhanced
 NEWS  6  OCT 22   WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT
                   Applications
 NEWS  7  OCT 24   CHEMLIST enhanced with intermediate list of
                   pre-registered REACH substances
 NEWS  8  NOV 21   CAS patent coverage to include exemplified prophetic
                   substances identified in English-, French-, German-,
                   and Japanese-language basic patents from 2004-present
 NEWS  9  NOV 26   MARPAT enhanced with FSORT command
 NEWS 10  NOV 26   MEDLINE year-end processing temporarily halts
                   availability of new fully-indexed citations
 NEWS 11  NOV 26   CHEMSAFE now available on STN Easy
 NEWS 12  NOV 26   Two new SET commands increase convenience of STN
                   searching
 NEWS 13  DEC 01   ChemPort single article sales feature unavailable
 NEWS 14  DEC 12   GBFULL now offers single source for full-text
                   coverage of complete UK patent families
 NEWS 15  DEC 17   Fifty-one pharmaceutical ingredients added to PS

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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 NEWS IPC8      For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
```

specific topic.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:18:08 ON 31 DEC 2008

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 12:18:28 ON 31 DEC 2008
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STRUCTURE FILE UPDATES: 30 DEC 2008 HIGHEST RN 1092172-37-6
DICTIONARY FILE UPDATES: 30 DEC 2008 HIGHEST RN 1092172-37-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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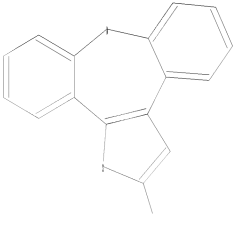

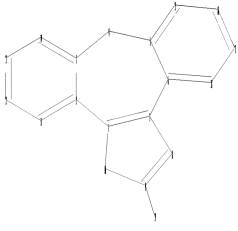

chain nodes :

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ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18
chain bonds :
9-19
ring bonds :
1-2  1-7  1-10  2-3  2-11  3-4  3-14  4-5  5-6  5-15  6-7  6-18  7-8  8-9  9-10
11-12  12-13  13-14  15-16  16-17  17-18
exact/norm bonds :
1-2  1-7  1-10  3-4  4-5  6-7  7-8  8-9  9-10
exact bonds :
9-19
normalized bonds :
2-3  2-11  3-14  5-6  5-15  6-18  11-12  12-13  13-14  15-16  16-17  17-18


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
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L1      STRUCTURE UPLOADED

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L1 HAS NO ANSWERS
L1              STR
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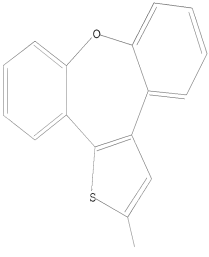


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Structure attributes must be viewed using STN Express query preparation.


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SAMPLE SEARCH INITIATED 12:19:07 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       75 TO ITERATE

100.0% PROCESSED       75 ITERATIONS                                6 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          981 TO     2019
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PROJECTED ANSWERS:               6 TO      266

L2            6 SEA SSS SAM L1

=> s l1 sss ful
FULL SEARCH INITIATED 12:19:12 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     1534 TO ITERATE

100.0% PROCESSED     1534 ITERATIONS                          147 ANSWERS
SEARCH TIME: 00.00.01

L3          147 SEA SSS FUL L1

=> fil cap
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             185.87     186.08

FILE 'CAPLUS' ENTERED AT 12:19:15 ON 31 DEC 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 31 Dec 2008  VOL 150 ISS 1
FILE LAST UPDATED: 30 Dec 2008  (20081230/ED)

Caplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/legal/infopolicy.html

=> s l3
L4             9 L3

=> d l4 1-9 ibib abs hitstr

L4   ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2008:493006  CAPLUS
DOCUMENT NUMBER:          148:472014
TITLE:                    Thienodibenzoazulene compounds as tumor necrosis
                          factor inhibitors and their preparation,
                          pharmaceutical compositions and use in the treatment
                          of inflammation
INVENTOR(S):              Mercep, Mladen; Mesic, Milan; Pesic, Dijana;
                          Zupanovic, Zeljko; Hrvacic, Boska
PATENT ASSIGNEE(S):       Pliva Farmaceutska Industrija, Dionicko Drustvo,
                          Croatia
SOURCE:                   U.S. Pat. Appl. Publ., 23pp., Cont.-in-part of Appl.
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No. PCT/HR2001/00027.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030153750	A1	20030814	US 2002-298217	20021118
US 6897211	B2	20050524		
HR 2000000310	A1	20020228	HR 2000-310	20000517
WO 2001087890	A1	20011122	WO 2001-HR27	20010516

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 20050171091	A1	20050804	US 2005-90743	20050325
PRIORITY APPLN. INFO.:			HR 2000-310 A	20000517
			WO 2001-HR27 A2	20010516
			US 2002-298217 A1	20021118

OTHER SOURCE(S): CASREACT 148:472014; MARPAT 148:472014
GI

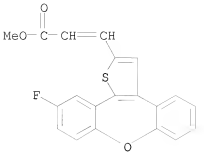
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to the dibenzoazulene compds. of formula I as well as to their pharmaceutical prepns. for the inhibition of tumor necrosis factor alpha (TNF-α) and interleukine 1 (IL-1) in mammal at all diseases and conditions where these mediators are excessively secreted. The compds. of the invention also demonstrate an analgetic action and can be used to relieve pain. Compds. of formula I wherein X is CH2, O, SO0-2 and NH and derivs.; R1-R9 are independently H, halo, C1-7 alkyl, alkenyl, (hetero)aryl, OH, C1-7 alkoxy, etc.; R10 is C2-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, (hetero)aryl, C1-15 haloalkyl, etc.; and their pharmaceutically acceptable salts and solvates thereof, are claimed. Example compound II•HCl was prepared by O-alkylation of 3-(8-oxa-1-thiadibenzo[e,h]azulene)methanol with 3-dimethylaminopropyl chloride. All the invention compds. were evaluated for their TNF-α inhibitory activity (some data given).

IT 374801-07-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate and intermediate; preparation of thienodibenzoazulene compds. as TNF inhibitors useful in the treatment of inflammation)

RN 374801-07-7 CAPLUS

CN 2-Propenoic acid, 3-(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)-, methyl ester (CA INDEX NAME)



IT 374801-08-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate and intermediate; preparation of thienodibenzoazulene compds. as TNF inhibitors useful in the treatment of inflammation)
RN 374801-08-8 CAPLUS
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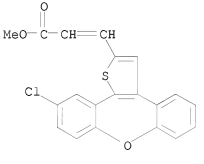
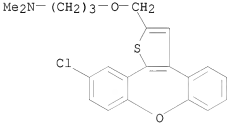
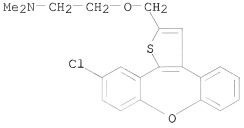


IT 374799-68-5P 374799-70-9P 374801-12-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of thienodibenzoazulene compds. as TNF inhibitors useful in the treatment of inflammation)
RN 374799-68-5 CAPLUS
CN 1-Propanamine, 3-[(11-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)

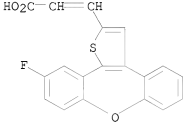


RN 374799-70-9 CAPLUS
CN Ethanamine, 2-[(11-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-

dimethyl- (CA INDEX NAME)



RN 374801-12-4 CAPLUS
CN 2-Propenoic acid, 3-(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)- (CA INDEX NAME)



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374801-09-9P 374801-10-2P 374801-13-5P
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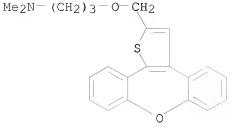
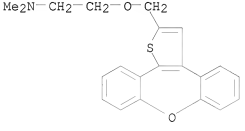
1019856-33-7P 1019856-42-8P 1019856-43-9P
1019856-44-0P 1019856-49-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of thienodibenzoazulene compds. as TNF inhibitors useful in the treatment of inflammation)
RN 374799-32-3 CAPLUS
CN 1-Propanamine, 3-(dibenzo[b,f]thieno[2,3-d]oxepin-2-ylmethoxy)-N,N-dimethyl-, hydrochloride (1:1) (CA INDEX NAME)



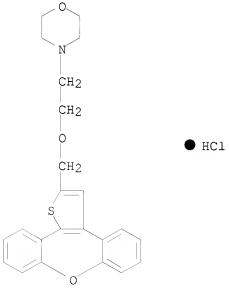
● HCl

RN 374799-37-8 CAPLUS
CN Ethanamine, 2-(dibenzo[b,f]thieno[2,3-d]oxepin-2-ylmethoxy)-N,N-dimethyl-, hydrochloride (1:1) (CA INDEX NAME)



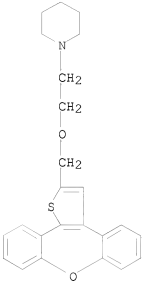
● HCl

RN 374799-41-4 CAPLUS
CN Morpholine, 4-[2-(dibenzo[b,f]thieno[3,2-d]oxepin-2-ylmethoxy)ethyl]-, hydrochloride (1:1) (CA INDEX NAME)



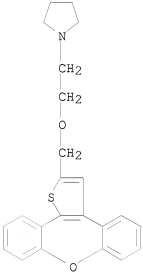
● HCl

RN 374799-47-0 CAPLUS
CN Piperidine, 1-[2-(dibenzo[b,f]thieno[3,2-d]oxepin-2-ylmethoxy)ethyl]-, hydrochloride (1:1) (CA INDEX NAME)



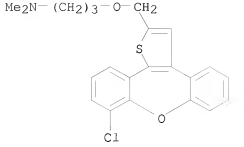
● HCl

RN 374799-51-6 CAPLUS
CN Pyrrolidine, 1-[2-(dibenzo[b,f]thieno[3,2-d]oxepin-2-ylmethoxy)ethyl]-, hydrochloride (1:1) (CA INDEX NAME)

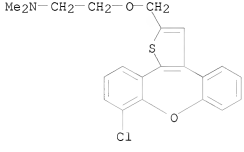


● HCl

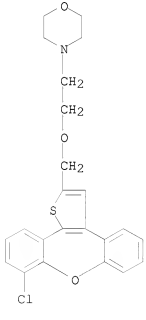
RN 374799-56-1 CAPLUS
CN 1-Propanamine, 3-[(9-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



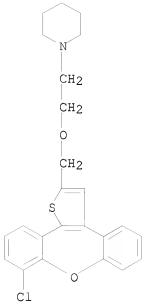
RN 374799-59-4 CAPLUS
CN Ethanamine, 2-[(9-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



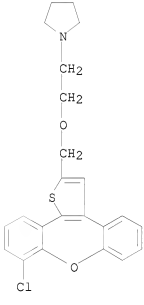
RN 374799-62-9 CAPLUS
CN Morpholine, 4-[2-[(9-chlorodibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



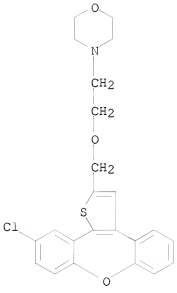
RN 374799-64-1 CAPLUS
CN Piperidine, 1-[2-[(9-chlorodibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



RN 374799-66-3 CAPLUS
CN Pyrrolidine, 1-[2-[(9-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



RN 374799-72-1 CAPLUS
CN Morpholine, 4-[2-[(11-chlorodibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



RN 374799-74-3 CAPLUS
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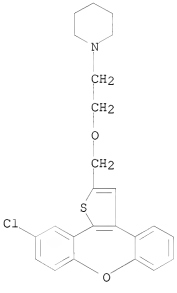
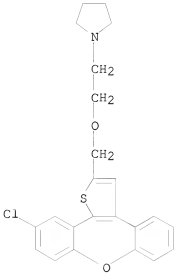
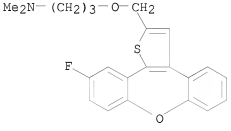


RN 374799-76-5 CAPLUS
CN Pyrrolidine, 1-[2-[(11-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)

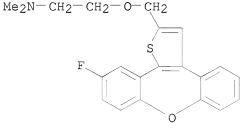


RN 374799-79-8 CAPLUS
CN 1-Propanamine, 3-[(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl-, hydrochloride (1:1) (CA INDEX NAME)



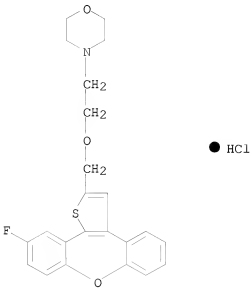
● HCl

RN 374799-83-4 CAPLUS
CN Ethanamine, 2-[(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl-, hydrochloride (1:1) (CA INDEX NAME)

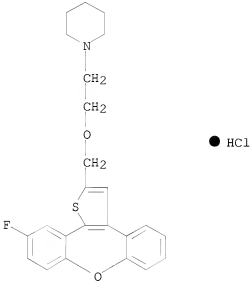


● HCl

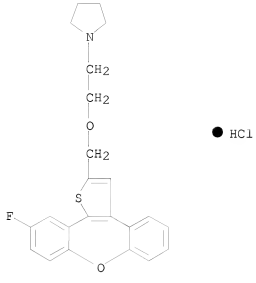
RN 374799-87-8 CAPLUS
CN Morpholine, 4-[2-[(11-fluorodibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]-, hydrochloride (1:1) (CA INDEX NAME)



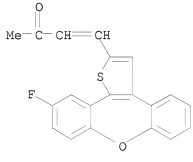
RN 374799-91-4 CAPLUS
CN Piperidine, 1-[2-[(11-fluorodibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]-, hydrochloride (1:1) (CA INDEX NAME)



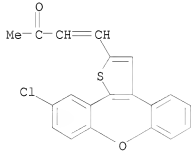
RN 374799-96-9 CAPLUS
CN Pyrrolidine, 1-[2-[(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]ethyl]-, hydrochloride (1:1) (CA INDEX NAME)



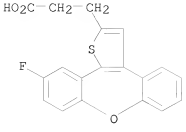
RN 374801-09-9 CAPLUS
CN 3-Buten-2-one, 4-(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)- (CA INDEX NAME)



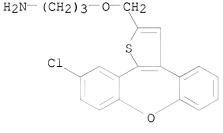
RN 374801-10-2 CAPLUS
CN 3-Buten-2-one, 4-(11-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)- (CA INDEX NAME)



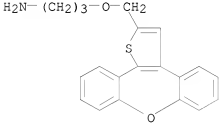
RN 374801-13-5 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-propanoic acid, 11-fluoro- (CA INDEX NAME)



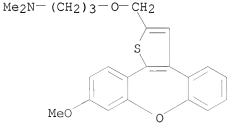
RN 1019856-07-5 CAPLUS
CN 1-Propanamine, 3-[(11-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-
(CA INDEX NAME)



RN 1019856-08-6 CAPLUS
CN 1-Propanamine, 3-(dibenzo[b,f]thieno[3,2-d]oxepin-2-ylmethoxy)- (CA INDEX NAME)

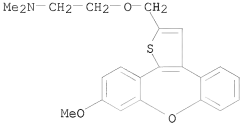


RN 1019856-16-6 CAPLUS
CN 1-Propanamine, 3-[(10-methoxydibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-
N,N-dimethyl- (CA INDEX NAME)

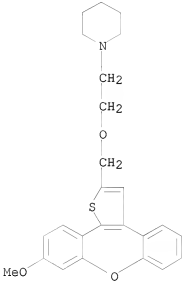


RN 1019856-17-7 CAPLUS
CN Ethanamine, 2-[(10-methoxydibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]-

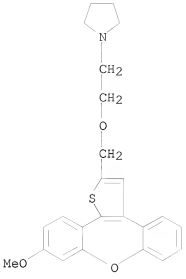
N,N-dimethyl- (CA INDEX NAME)



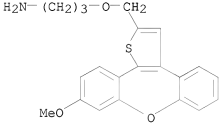
RN 1019856-18-8 CAPLUS
CN Piperidine, 1-[2-[(10-methoxydibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



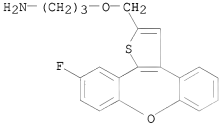
RN 1019856-19-9 CAPLUS
CN Pyrrolidine, 1-[2-[(10-methoxydibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



RN 1019856-20-2 CAPLUS
CN 1-Propanamine, 3-[(10-methoxydibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]-
(CA INDEX NAME)

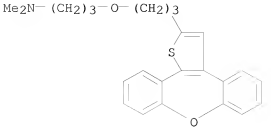


RN 1019856-30-4 CAPLUS
CN 1-Propanamine, 3-[(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-
, hydrochloride (1:1) (CA INDEX NAME)

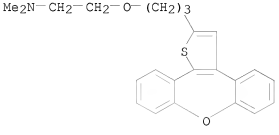


● HCl

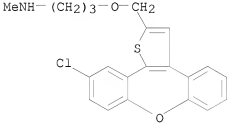
RN 1019856-32-6 CAPLUS
CN 1-Propanamine, 3-(3-dibenzo[b,f]thieno[3,2-d]oxepin-2-ylpropoxy)-N,N-
dimethyl- (CA INDEX NAME)



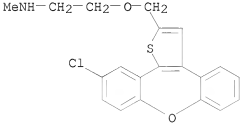
RN 1019856-33-7 CAPLUS
CN Ethanamine, 2-(3-dibenzo[b,f]thieno[2,3-d]oxepin-2-ylpropoxy)-N,N-dimethyl- (CA INDEX NAME)



RN 1019856-42-8 CAPLUS
CN 1-Propanamine, 3-[(11-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N-methyl- (CA INDEX NAME)

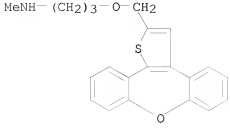


RN 1019856-43-9 CAPLUS
CN Ethanamine, 2-[(11-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N-methyl- (CA INDEX NAME)

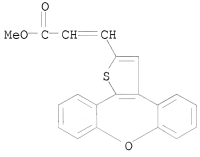


RN 1019856-44-0 CAPLUS
CN 1-Propanamine, 3-(dibenzo[b,f]thieno[2,3-d]oxepin-2-ylmethoxy)-N-methyl-

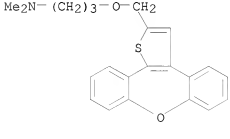
(CA INDEX NAME)



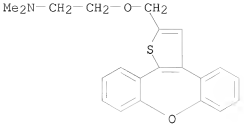
RN 1019856-49-5 CAPLUS
CN 2-Propenoic acid, 3-dibenzo[b,f]thieno[3,2-d]oxepin-2-yl-, methyl ester
(CA INDEX NAME)



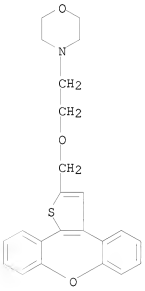
IT 374799-34-5P 374799-39-0P 374799-44-7P
374799-49-2P 374799-54-9P 374799-81-2P
374799-85-6P 374799-89-0P 374799-94-7P
374799-98-1P 374801-15-7P 374801-16-8P
374801-17-9P 374801-18-0P 374801-37-3P
374801-40-8P 1019856-51-9P 1019856-59-7P
1019856-66-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(intermediate; preparation of thienodibenzoazulene compds. as TNF inhibitors
useful in the treatment of inflammation)
RN 374799-34-5 CAPLUS
CN 1-Propanamine, 3-(dibenzo[b,f]thieno[2,3-d]oxepin-2-ylmethoxy)-N,N-
dimethyl- (CA INDEX NAME)



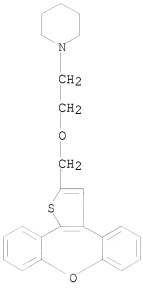
RN 374799-39-0 CAPLUS
CN Ethanamine, 2-(dibenzo[b,f]thieno[2,3-d]oxepin-2-ylmethoxy)-N,N-dimethyl-
(CA INDEX NAME)



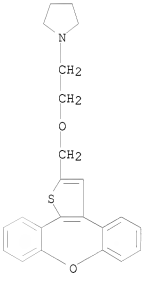
RN 374799-44-7 CAPLUS
CN Morpholine, 4-[2-(dibenzo[b,f]thieno[3,2-d]oxepin-2-ylmethoxy)ethyl]- (CA INDEX NAME)



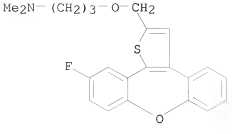
RN 374799-49-2 CAPLUS
CN Piperidine, 1-[2-(dibenzo[b,f]thieno[3,2-d]oxepin-2-ylmethoxy)ethyl]- (CA INDEX NAME)



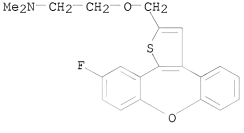
RN 374799-54-9 CAPLUS
CN Pyrrolidine, 1-[2-(dibenzo[b,f]thieno[3,2-d]oxepin-2-ylmethoxy)ethyl]-
(CA INDEX NAME)



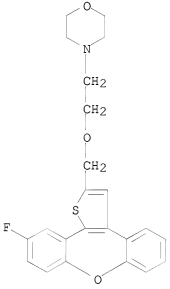
RN 374799-81-2 CAPLUS
CN 1-Propanamine, 3-[(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-
N,N-dimethyl- (CA INDEX NAME)



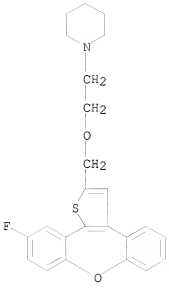
RN 374799-85-6 CAPLUS
CN Ethanamine, 2-[(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



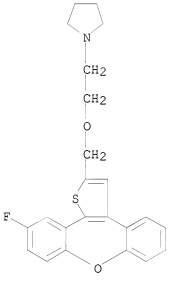
RN 374799-89-0 CAPLUS
CN Morpholine, 4-[2-[(11-fluorodibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



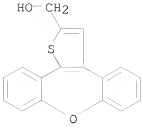
RN 374799-94-7 CAPLUS
CN Piperidine, 1-[2-[(11-fluorodibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



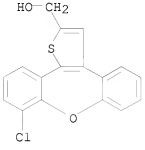
RN 374799-98-1 CAPLUS
CN Pyrrolidine, 1-[2-[(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



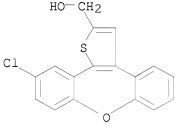
RN 374801-15-7 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-methanol (CA INDEX NAME)



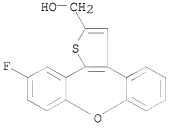
RN 374801-16-8 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-methanol, 9-chloro- (CA INDEX NAME)



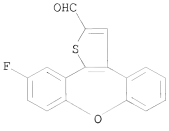
RN 374801-17-9 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-methanol, 11-chloro- (CA INDEX NAME)



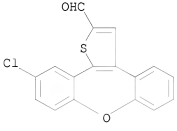
RN 374801-18-0 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-methanol, 11-fluoro- (CA INDEX NAME)



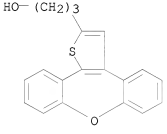
RN 374801-37-3 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxaldehyde, 11-fluoro- (CA INDEX NAME)



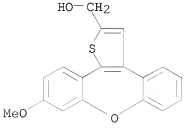
RN 374801-40-8 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxaldehyde, 11-chloro- (CA INDEX NAME)



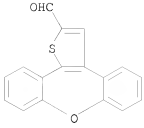
RN 1019856-51-9 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-propanol (CA INDEX NAME)



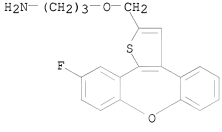
RN 1019856-59-7 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-methanol, 10-methoxy- (CA INDEX NAME)



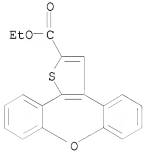
RN 1019856-66-6 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxaldehyde (CA INDEX NAME)



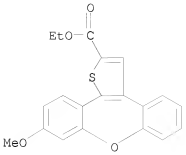
IT 1019856-92-8P
RL: PRPH (Prophetic); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prophetic intermediate; preparation of thienodibenzoazulene compds. as TNF inhibitors useful in the treatment of inflammation)
RN 1019856-92-8 CAPLUS
CN 1-Propanamine, 3-[(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]- (CA INDEX NAME)



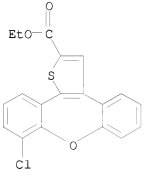
IT 62551-05-7 756480-99-6 1019856-69-9
1019856-71-3 1019856-73-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of thienodibenzoazulene compds. as TNF inhibitors useful in the treatment of inflammation)
RN 62551-05-7 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxylic acid, ethyl ester (CA INDEX NAME)



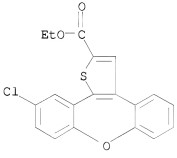
RN 756480-99-6 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 10-methoxy-, ethyl ester (CA INDEX NAME)



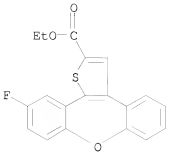
RN 1019856-69-9 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 9-chloro-, ethyl ester (CA INDEX NAME)



RN 1019856-71-3 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-chloro-, ethyl ester (CA INDEX NAME)



RN 1019856-73-5 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-fluoro-, ethyl ester (CA INDEX NAME)



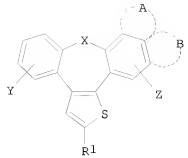
L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:959196 CAPLUS
DOCUMENT NUMBER: 147:322957
TITLE: Preparation of 1- or 3-thia-benzonaphthoazulenes as inhibitors of tumor necrosis factor production and intermediates for the preparation thereof
INVENTOR(S): Mercep, Mladen; Mesic, Milan; Pesic, Dijana; Ozimec, Ivana; Trojko, Rudolf
PATENT ASSIGNEE(S): Glaxosmith Kline Istrazivocki Centar Zagreb, D.O.O., Croatia
SOURCE: U.S., 18pp., Cont.-in-part of Appl. No. PCT/HR03/00014.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 7262309	B2	20070828	US 2004-963979	20041012
US 20050130964	A1	20050616		
HR 2002000303	B1	20070531	HR 2002-303	20020410
WO 2003084961	A1	20031016	WO 2003-HR14	20030409

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: HR 2002-303 A 20020410
WO 2003-HR14 A2 20030409

OTHER SOURCE(S): MARPAT 147:322957
GI



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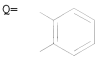
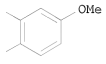




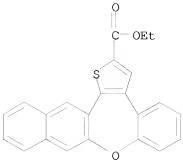
AB The present invention relates to benzonaphthoazulene derivs. of thiophene class [I; X = CH2, O, S, S(:O), S(:O)2, or (un)protected NH; Y, Z = H, halogen, C1-4 alkyl, C2-4 alkenyl, C2-4 alkynyl, CF3, halo-C1-4 alkyl, HO, C1-4 alkoxy, CF3O, C1-4 alkanoyl, NH2, amino-C1-4 alkyl, C1-4 alkylamino, N-(C1-4 alkyl)amino, N,N-di(C1-4 alkyl)amino, SH, C1-4 alkylthio, C1-4 alkylsulfonyl, C1-4 alkylsulfinyl, CO2H, C1-4 alkoxycarbonyl, NO2; one of the ring A and B is present while is the other one is absent, and is selected from the group consisting of Q, Q1, and Q2; R1 = (un)substituted C1-7 alkyl, C1-7 alkyloxycarbonyl, (CH2)m-Q3-(CH2)n-Q4-NR2R3; wherein R2, R3 = H, C1-4 alkyl, or aryl or NR2R3 taken together forms (un)substituted heterocyclyl or heteroaryl; n = an integer of 0-3; m = an integer of 1-3; Q3, Q4 = O, S, C(y1)(y2), N(y1), C(y1):CH, C.tplbond.C; y1, y2 = H, halogen, HO, C1-4 alkoxy, C1-4 alkanoyl, SH, C1-4 alkylthio, C1-4 alkylsulfonyl, C1-4 alkylsulfinyl, NO2, etc.; or y1 and y2 taken together with the carbon atom to which they are attached form carbonyl or imino group] and their pharmacol. acceptable salts and solvates. These compds. inhibit the production of tumor necrosis factor-α (TNF-α) and interleukin-1 (IL-1), possess antiinflammatory or analgetic effects, and are useful for treating inflammation associated with TNF-α, in particular rheumatoid arthritis. Thus, Et 2-mercaptoacetate (0.005 mol) and triethylamine (1.0 mL) were added to a solution of 12-chloro-5-oxabenzo[4,5]cyclohepta[1,2-b]naphthalene-13-carboxaldehyde (0.005 mol) in 10 mL pyridine and the mixture was refluxed under stirring for 3 h to give 8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulene-2-carboxylic acid Et ester as a white solid. Two compds., namely dimethyl[2-(8-oxa-1-thiabenzo[e]naphtho[1,2-h]azulen-2-ylmethoxy)ethyl]amine and dimethyl[3-(11-methoxy-8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulen-2-ylmethoxy)propyl]amine, showed activity in at least two investigated assays selected from (1) inhibitory action on TNF-α and IL-1 secretion in human peripheral blood mononuclear cells or mouse peritoneal macrophages, resp., in vitro, (2) inhibitory action on LPS-induced excessive TNF-α or IL-1 secretion in mice, (3) writhing assay for analgetic activity in mice, and (4) LPS-induced shock in mice.

IT 613671-14-0P, 8-Oxa-1-thiabenzo[e]naphtho[3,2-h]azulene-2-carboxylic acid ethyl ester 613671-17-3P, 8-Oxa-1-thiabenzo[e]naphtho[1,2-h]azulene-2-carboxylic acid ethyl ester 613671-18-4P, 11-Methoxy-8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulene-2-carboxylic acid ethyl ester 613671-19-5P, 9,10,11,12-Tetrahydro-8-oxa-1-thiabenzo[e]naphtho[1,2-h]azulene-2-carboxylic acid ethyl ester 613671-20-8P, 10,11,12,13-Tetrahydro-8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulene-2-

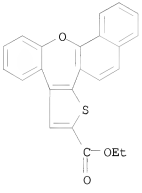
carboxylic acid ethyl ester 613671-21-9P,
(8-Oxa-1-thiabenzo[e]naphtho[3,2-h]azulen-2-yl)methanol
613671-24-2P, (8-Oxa-1-thiabenzo[e]naphtho[1,2-h]azulen-2-
yl)methanol 613671-25-3P,
(11-Methoxy-8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulen-2-yl)methanol
613671-26-4P, (9,10,11,12-Tetrahydro-8-oxa-1-
thiabenzo[e]naphtho[1,2-h]azulen-2-yl)methanol 613671-27-5P,
(10,11,12,13-Tetrahydro-8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulen-2-
yl)methanol 613671-28-6P,
Dimethyl[2-[(8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulen-2-
yl)methoxy]ethyl]amine 613671-29-7P,
Dimethyl[3-[(8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulen-2-
yl)methoxy]propyl]amine 613671-30-0P,
[3-[(8-Oxa-1-thiabenzo[e]naphtho[3,2-h]azulen-2-yl)methoxy]propyl]amine
613671-34-4P, Dimethyl[2-[(8-oxa-1-thiabenzo[e]naphtho[1,2-
h]azulen-2-yl)methoxy]ethyl]amine 613671-35-5P,
Dimethyl[3-[(8-oxa-1-thiabenzo[e]naphtho[1,2-h]azulen-2-
yl)methoxy]propyl]amine 613671-36-6P,
Dimethyl[3-[(11-methoxy-8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulen-2-
yl)methoxy]propyl]amine 613671-37-7P,
Dimethyl[2-[(9,10,11,12-tetrahydro-8-oxa-1-thiabenzo[e]naphtho[1,2-
h]azulen-2-yl)methoxy]ethyl]amine 613671-38-8P,
Dimethyl[3-[(9,10,11,12-tetrahydro-8-oxa-1-thiabenzo[e]naphtho[1,2-
h]azulen-2-yl)methoxy]propyl]amine 613671-39-9P,
[3-[(9,10,11,12-Tetrahydro-10-oxa-3-thiabenzo[e]naphtho[1,2-h]azulen-2-
yl)methoxy]propyl]amine 613671-40-2P,
(Methyl)[3-[(9,10,11,12-tetrahydro-8-oxa-1-thiabenzo[e]naphtho[1,2-
h]azulen-2-yl)methoxy]propyl]amine 613671-41-3P,
Dimethyl[2-[(10,11,12,13-tetrahydro-8-oxa-1-thiabenzo[e]naphtho[3,2-
h]azulen-2-yl)methoxy]ethyl]amine 613671-42-4P,
Dimethyl[3-[(10,11,12,13-tetrahydro-8-oxa-1-thiabenzo[e]naphtho[3,2-
h]azulen-2-yl)methoxy]propyl]amine 613671-43-5P,
4-[2-[(10,11,12,13-Tetrahydro-8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulen-2-
yl)methoxy]ethyl]morpholine 613671-44-6P,
1-[2-[(10,11,12,13-Tetrahydro-8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulen-2-
yl)methoxy]ethyl]piperidine 613671-45-7P,
1-[2-[(10,11,12,13-Tetrahydro-8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulen-2-
yl)methoxy]ethyl]pyrrolidine 613671-46-8P,
Dimethyl[1-methyl-2-[(10,11,12,13-tetrahydro-8-oxa-1-
thiabenzo[e]naphtho[3,2-h]azulen-2-yl)methoxy]ethyl]amine
613671-61-7P, Dimethyl[2-[(10,11,12,13-tetrahydro-8-oxa-1-
thiabenzo[e]naphtho[3,2-h]azulen-2-yl)methoxy]propyl]amine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of 1- or 3-thia-benzonaphthoazuleness as inhibitors of tumor
necrosis factor production for treating inflammation and rheumatoid
arthritis)

RN 613671-14-0 CAPLUS

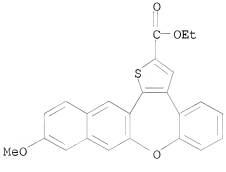
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-carboxylic acid, ethyl ester
(CA INDEX NAME)



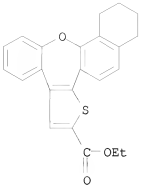
RN 613671-17-3 CAPLUS
CN Benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-carboxylic acid, ethyl ester (CA INDEX NAME)



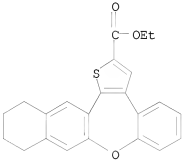
RN 613671-18-4 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-methoxy-, ethyl ester (CA INDEX NAME)



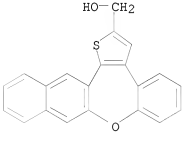
RN 613671-19-5 CAPLUS
CN Benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-carboxylic acid, 1,2,3,4-tetrahydro-, ethyl ester (CA INDEX NAME)



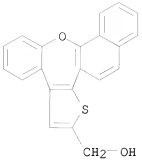
RN 613671-20-8 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-carboxylic acid, 10,11,12,13-tetrahydro-, ethyl ester (CA INDEX NAME)



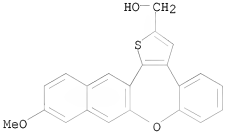
RN 613671-21-9 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-methanol (CA INDEX NAME)



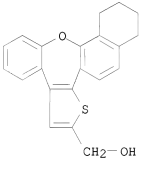
RN 613671-24-2 CAPLUS
CN Benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-methanol (CA INDEX NAME)



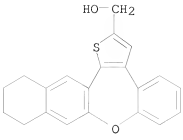
RN 613671-25-3 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-methanol, 11-methoxy- (CA INDEX NAME)



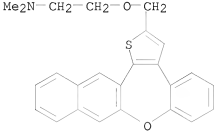
RN 613671-26-4 CAPLUS
CN Benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-methanol, 1,2,3,4-tetrahydro- (CA INDEX NAME)



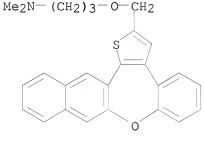
RN 613671-27-5 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-methanol, 10,11,12,13-tetrahydro- (CA INDEX NAME)



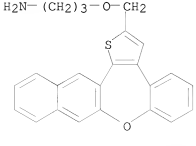
RN 613671-28-6 CAPLUS
CN Ethanamine, 2-(benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)



RN 613671-29-7 CAPLUS
CN 1-Propanamine, 3-(benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)

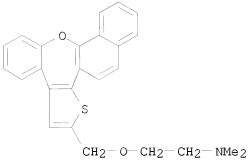


RN 613671-30-0 CAPLUS
CN 1-Propanamine, 3-(benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-ylmethoxy)- (CA INDEX NAME)

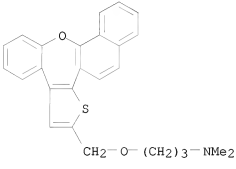


RN 613671-34-4 CAPLUS
CN Ethanamine, 2-(benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-ylmethoxy)-N,N-

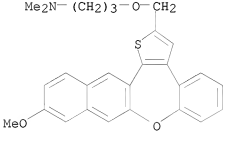
dimethyl- (CA INDEX NAME)



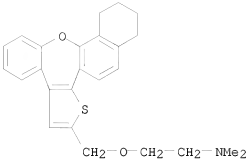
RN 613671-35-5 CAPLUS
CN 1-Propanamine, 3-(benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)



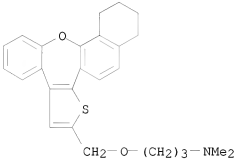
RN 613671-36-6 CAPLUS
CN 1-Propanamine, 3-[(11-methoxybenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



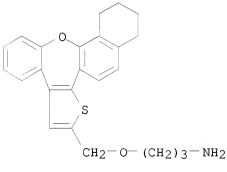
RN 613671-37-7 CAPLUS
CN Ethanamine, N,N-dimethyl-2-[(1,2,3,4-tetrahydrobenzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-yl)methoxy]- (CA INDEX NAME)



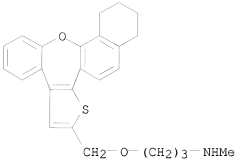
RN 613671-38-8 CAPLUS
CN 1-Propanamine, N,N-dimethyl-3-[(1,2,3,4-tetrahydrobenzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-yl)methoxy]- (CA INDEX NAME)



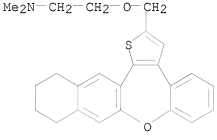
RN 613671-39-9 CAPLUS
CN 1-Propanamine, 3-[(1,2,3,4-tetrahydrobenzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-yl)methoxy]- (CA INDEX NAME)



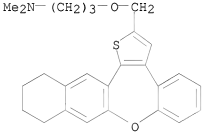
RN 613671-40-2 CAPLUS
CN 1-Propanamine, N-methyl-3-[(1,2,3,4-tetrahydrobenzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-yl)methoxy]- (CA INDEX NAME)



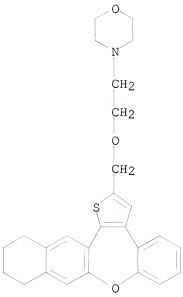
RN 613671-41-3 CAPLUS
CN Ethanamine, N,N-dimethyl-2-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]- (CA INDEX NAME)



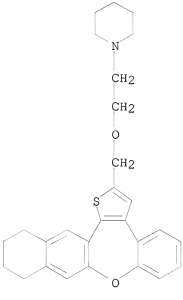
RN 613671-42-4 CAPLUS
CN 1-Propanamine, N,N-dimethyl-3-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]- (CA INDEX NAME)



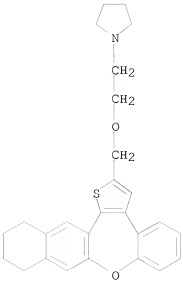
RN 613671-43-5 CAPLUS
CN Morpholine, 4-[2-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



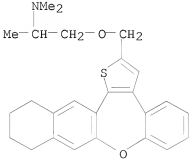
RN 613671-44-6 CAPLUS
CN Piperidine, 1-[2-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



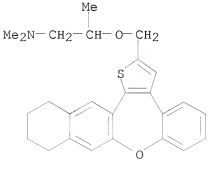
RN 613671-45-7 CAPLUS
CN Pyrrolidine, 1-[2-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



RN 613671-46-8 CAPLUS
CN 2-Propanamine, N,N-dimethyl-1-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]- (CA INDEX NAME)



RN 613671-61-7 CAPLUS
CN 1-Propanamine, N,N-dimethyl-2-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]- (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1093338 CAPLUS
DOCUMENT NUMBER: 145:438595
TITLE: Tetracyclic dibenzo[e,h]azulenes as monoamine reuptake inhibitors, their preparation, pharmaceutical compositions, and use for treatment of CNS diseases and disorders
INVENTOR(S): Mesic, Milan; Mercep, Mladen; Pesic, Dijana; Rupcic, Renata; Stanic, Barbara
PATENT ASSIGNEE(S): Glaxosmithkline Istrazivacki Centar Zagreb D.O.O., Croatia
SOURCE: PCT Int. Appl., 69pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006109190	A1	20061019	WO 2006-IB1480	20060201
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1846414	A1	20071024	EP 2006-765463	20060201
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR				
JP 2008528677	T	20080731	JP 2007-553745	20060201
PRIORITY APPLN. INFO.:			US 2005-649807P	P 20050202
			WO 2006-IB1480	W 20060201

OTHER SOURCE(S): MARPAT 145:438595
GI

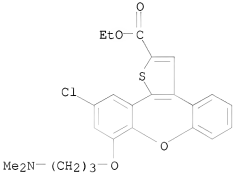
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to tetracyclic dibenzo[e,h]azulene compds. of formula I, which are monoamine reuptake inhibitors. In compds. I, X is CH2, O, S, or N(R6), where R6 is H, C1-4 alkyl, C7-10 arylalkyl, C2-5 alkanoyl, C7-10 aroyl, or C2-7 alkoxycarbonyl; W and Z are independently selected from O, S, aromatic CH, and N(R6); R1 is selected from alkyl, alkoxy, alkylthio, alkylamino, alkenyl, alkynyl, alkoxyalkyl, alkylthioalkyl, alkylaminoalkyl, etc.; R2 is halo, preferably chloro or fluoro; and R3, R4, and R5 are independently selected from H, halo, OH, carboxy, (un)substituted C1-7 alkyl, C1-7 alkoxy, (un)substituted C1-7 alkoxycarbonyl, (un)substituted C7-10 aryloxycarbonyl, etc.; provided that W and Z can not simultaneously be O, S, or an aromatic CH. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of a compound I with at least one pharmaceutically acceptable carrier or diluent, as well as to the use of the compns. for the treatment of CNS diseases and disorders. Substitution

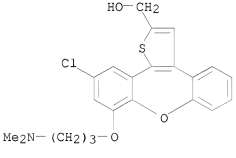
of (2-chlorophenyl)acetic acid with 4-chloro-2-methoxyphenol followed by cyclization gave oxepinone II, which underwent chlorination and formylation resulting in the formation of III. Chloroaldehyde III was cyclized with Et mercaptoacetate followed by demethylation and substitution of 3-(dimethylamino)propyl chloride to give dibenzo[e,h]azulene IV. The compds. of the invention, e.g., IV, express IC50 values of less than 1 μM for binding affinity to serotonin, dopamine, and norepinephrine transporters.

IT 912853-08-8P 912853-10-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of tetracyclic dibenzoazulenes as monoamine reuptake inhibitors useful in treatment of CNS diseases)

RN 912853-08-8 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-chloro-9-[3-(dimethylamino)propoxy]-, ethyl ester (CA INDEX NAME)



RN 912853-10-2 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-methanol, 11-chloro-9-[3-(dimethylamino)propoxy]- (CA INDEX NAME)

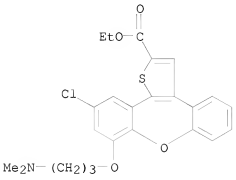


IT 912853-09-9P 912853-11-3P 912853-12-4P
912853-13-5P 912853-14-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of tetracyclic dibenzoazulenes as monoamine reuptake inhibitors useful in treatment of CNS diseases)

RN 912853-09-9 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-chloro-9-[3-(dimethylamino)propoxy]-, ethyl ester, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (CA INDEX NAME)

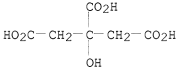
CM 1

CRN 912853-08-8
CMF C24 H24 Cl N O4 S

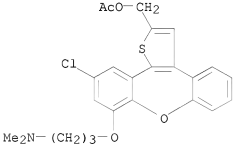


CM 2

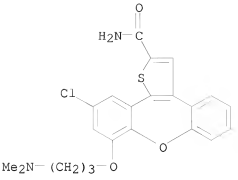
CRN 77-92-9
CMF C6 H8 O7



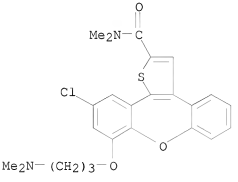
RN 912853-11-3 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-methanol,
11-chloro-9-[3-(dimethylamino)propoxy]-, 2-acetate (CA INDEX NAME)



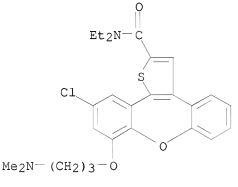
RN 912853-12-4 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxamide,
11-chloro-9-[3-(dimethylamino)propoxy]- (CA INDEX NAME)



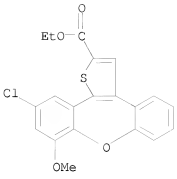
RN 912853-13-5 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxamide,
11-chloro-9-[3-(dimethylamino)propoxy]-N,N-dimethyl- (CA INDEX NAME)



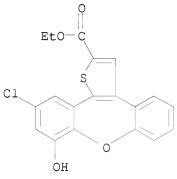
RN 912853-14-6 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxamide,
11-chloro-9-[3-(dimethylamino)propoxy]-N,N-diethyl- (CA INDEX NAME)



IT 912853-06-6P 912853-07-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of tetracyclic dibenzoazulenes as monoamine reuptake inhibitors useful in treatment of CNS diseases)
RN 912853-06-6 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-chloro-9-methoxy-, ethyl ester (CA INDEX NAME)



RN 912853-07-7 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxylic acid, 11-chloro-9-hydroxy-, ethyl ester (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:710823 CAPLUS
DOCUMENT NUMBER: 145:145984
TITLE: Preparation of anti-inflammatory erythromycin macrolide conjugates
INVENTOR(S): Mercep, Mladen; Mesic, Milan; Markovic, Stribor; Pesic, Dijana; Ozimec Landak, Ivana; Komac, Marijana; Makaruha Stegic, Oresta; Selmani, Selvira; Banjanac, Mihailo
PATENT ASSIGNEE(S): Pliva-Istrazivacki Institut D.O.O., Croatia; Glaxosmithkline Istrazivacki Centar Zagreb D.O.O.
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006075255	A2	20060720	WO 2006-IB1079	20060113
WO 2006075255	A3	20061026		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,

KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

EP 1844053 A2 20071017 EP 2006-727557 20060113

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,
BA, HR, MK, YU

JP 2008532927 T 20080821 JP 2007-550873 20060113

US 20080096830 A1 20080424 US 2007-813882 20070713

PRIORITY APPLN. INFO.: US 2005-643931P P 20050113

WO 2006-IB1079 W 20060113

OTHER SOURCE(S): CASREACT 145:145984; MARPAT 145:145984

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates (a) to new compds. represented by formula M-L-D: wherein M represents a macrolide subunit (macrolide moiety) derived from macrolide possessing the property of accumulation in inflammatory cells, D represents a dibenzo[e/z]azulene subunit with anti-inflammatory, analgesic and/or antipyretic activity and L represents a linking group covalently linking M and D; (b) to their pharmacol. acceptable salts, prodrugs and solvates, (c) to processes and intermediates for their preparation, and (d) to their use in the treatment of inflammatory diseases and conditions in humans and animals. Thus, macrolide conjugate I was prepared and tested in mice and in vitro as antiinflammatory agent, wherein the inflammatory process comprises pro-inflammatory cytokine production, the method further comprising exposing human peripheral leukocytes to an amount of compound effective to reduce production of at least one of TNF-α, IL-1α, IL-1β, IL-6, IL-8, IL-2, IL-5, and IFN-α, compared to control leukocytes.

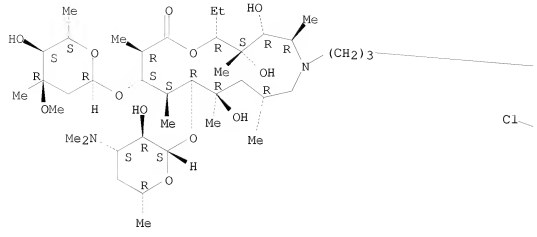
IT 899810-13-0P 899810-15-2P 899810-16-3P
899810-17-4P 899810-18-5P 899810-19-6P
899810-25-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antiinflamatory erythromycin macrolide conjugates)

RN 899810-13-0 CAPLUS

CN 1-Oxa-6-azacyclopentadecan-15-one,
6-[3-[[(11-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methyl]amino]propyl]-13-[(2,6-dideoxy-3-C-methyl-3-O-methyl-α-L-ribo-hexopyranosyl)oxy]-2-ethyl-3,4,10-trihydroxy-3,5,8,10,12,14-hexamethyl-11-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-xylo-hexopyranosyl]oxy]-,
(2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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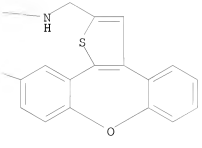
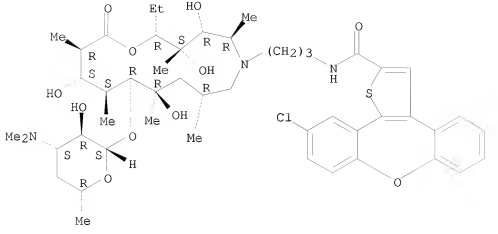


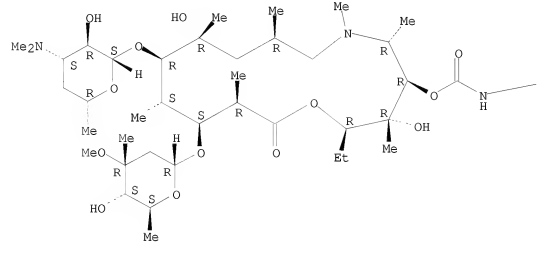
RN 899810-15-2 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxamide, 11-chloro-N-[3-[(2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-2-ethyl-3,4,10,13-tetrahydroxy-3,5,8,10,12,14-hexamethyl-15-oxo-11-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-xylo-hexopyranosyl]oxy]-1-oxa-6-azacyclopentadec-6-yl]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 899810-16-3 CAPLUS
CN Carbamic acid, [4-[[(11-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)carbonyl]amino]butyl]-, (2R,3R,4R,5R,8R,10R,11R,12S,13S,14R)-13-[(2,6-dideoxy-3-C-methyl-3-O-methyl-α-L-ribo-hexopyranosyl)oxy]-2-ethyl-3,10-dihydroxy-3,5,6,8,10,12,14-heptamethyl-15-oxo-11-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-xylo-hexopyranosyl]oxy]-1-oxa-6-azacyclopentadec-4-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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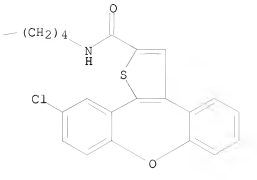
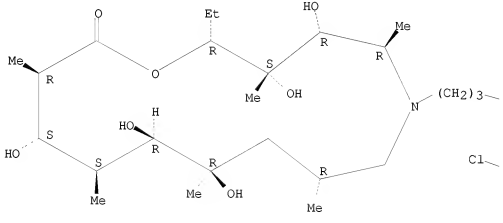
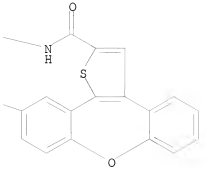


RN 899810-17-4 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxamide, 11-chloro-N-[3-[(2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-2-ethyl-3,4,10,11,13-pentahydroxy-3,5,8,10,12,14-hexamethyl-15-oxo-1-oxa-6-azacyclopentadec-6-yl]propyl]- (CA INDEX NAME)

Absolute stereochemistry.

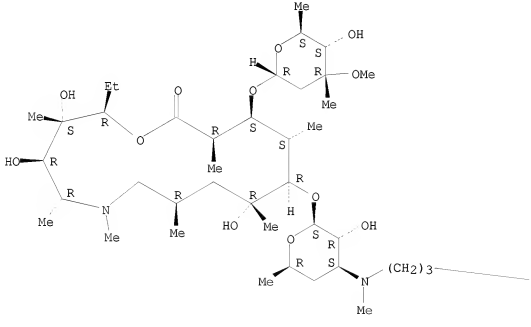
PAGE 1-A





RN 899810-18-5 CAPLUS
CN 1-Oxa-6-azacyclopentadecan-15-one, 11-[[3-[[3-[[(11-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)carbonyl]amino]propyl]methylamino]-3,4,6-trideoxy-β-D-xylo-hexopyranosyl]oxy]-13-[(2,6-dideoxy-3-C-methyl-3-O-methyl-α-L-ribo-hexopyranosyl)oxy]-2-ethyl-3,4,10-trihydroxy-3,5,6,8,10,12,14-heptamethyl-, (2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)- (CA INDEX NAME)

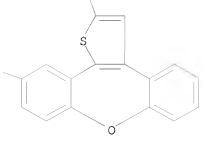
Absolute stereochemistry.



PAGE 1-B

PAGE 2-A

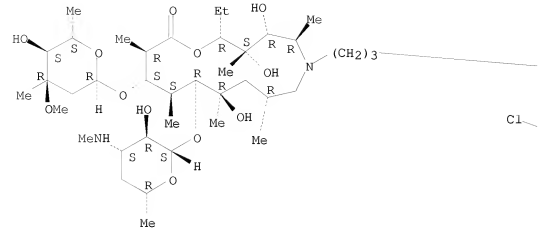
PAGE 2-B



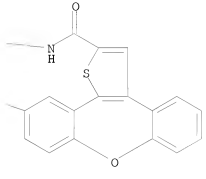
RN 899810-19-6 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxamide, 11-chloro-N-[3-[(2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-13-[(2,6-dideoxy-3-C-methyl-3-O-methyl-α-L-ribo-hexopyranosyl)oxy]-2-ethyl-3,4,10-trihydroxy-3,5,8,10,12,14-hexamethyl-15-oxo-11-[[3,4,6-trideoxy-3-(methylamino)-β-D-xylo-hexopyranosyl]oxy]-1-oxa-6-azacyclopentadec-6-yl]propyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



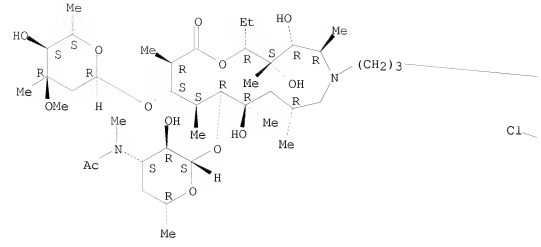
PAGE 1-B



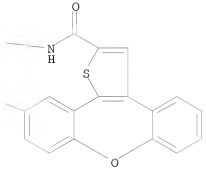
RN 899810-25-4 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxamide, N-[3-[(2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-11-[[3-(acetylmethylamino)-3,4,6-trideoxy-β-D-xylo-hexopyranosyl]oxy]-13-[(2,6-dideoxy-3-C-methyl-3-O-methyl-α-L-ribo-hexopyranosyl)oxy]-2-ethyl-3,4,10-trihydroxy-3,5,8,10,12,14-hexamethyl-15-oxo-1-oxa-6-azacyclopentadec-6-yl]propyl]-11-chloro- (CA INDEX NAME)

Absolute stereochemistry.

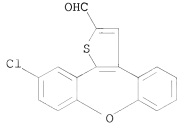
PAGE 1-A



PAGE 1-B

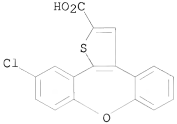


IT 374801-40-8 756481-06-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of antiinflamatory erythromycin macrolide conjugates)
RN 374801-40-8 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxaldehyde, 11-chloro- (CA INDEX NAME)



RN 756481-06-8 CAPLUS

CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-chloro- (CA INDEX NAME)



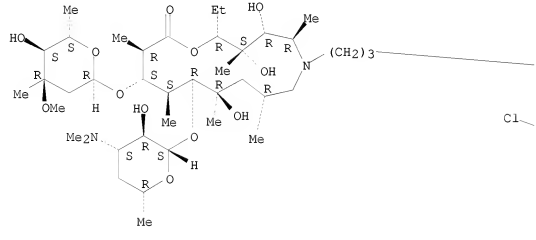
IT 899810-14-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of antiinflamatory erythromycin macrolide conjugates)

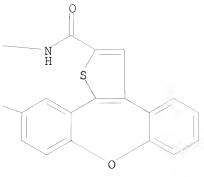
RN 899810-14-1 CAPLUS

CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxamide, 11-chloro-N-[3-[(2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-13-[(2,6-dideoxy-3-C-methyl-3-O-methyl-α-L-ribo-hexopyranosyl)oxy]-2-ethyl-3,4,10-trihydroxy-3,5,8,10,12,14-hexamethyl-15-oxo-11-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-xylo-hexopyranosyl]oxy]-1-oxa-6-azacyclopentadec-6-yl]propyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:729528 CAPLUS
DOCUMENT NUMBER: 143:179664
TITLE: Benzonaphthoazulenes for the manufacture of pharmaceutical formulations for the treatment and prevention of central nervous system diseases and disorders
INVENTOR(S): Mercep, Mladen; Mesic, Milan; Pesic, Dijana; Ozimeclandek, Ivana; Trojko, Rudolf; Rupcic, Renata
PATENT ASSIGNEE(S): Pliva-Istrazivacki Institut D.O.O., Croatia
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005072728	A1	20050811	WO 2005-HR8	20050127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2554886	A1	20050811	CA 2005-2554886	20050127
EP 1708696	A1	20061011	EP 2005-702165	20050127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
CN 1938016	A	20070328	CN 2005-80010392	20050127
JP 2007519698	T	20070719	JP 2006-550310	20050127
IN 2006DN04130	A	20070817	IN 2006-DN4130	20060718
US 20070173499	A1	20070726	US 2006-587823	20061220
PRIORITY APPLN. INFO.:			HR 2004-104 A	20040130

OTHER SOURCE(S): MARPAT 143:179664

AB The present invention relates to the use of compds. from the group of benzonaphthoazenes and of their pharmaceutically acceptable salts and solvates for the manufacture of a pharmaceutical formulation for the treatment and prevention of diseases, damages and disorders of the central nervous system (CNS) caused by disorders of the neurochem. equilibrium of biogenic amines or other transmitters. Thus, in vitro affinity of benzonaphthoazulenes for binding to recombinant human 5-HT2A and 5-HT2C serotonin receptors expressed in CHO-K1 or COS-7 cells was determined using a radioligand. The radioligand binding was inhibited by the test compds. proportionally to the affinity of a certain compound for the receptor and to the concentration of the compound Compds. showing IC50 and Ki in concns. lower than 1 μM were considered to be active. Compound dimethyl-[3-(1,8-dithia-benzo[e]naphtho[3,2-h]azulen-2-ylmethoxy)-propyl]-amine and dimethyl-[3-(3, 10-dithia-benzo[e]naphtho[1,2-h]azulen-2-ylmethoxy)-propyl]-amine showed binding affinity to 5-HT2A and 5-HT2C serotonin receptors expressed as IC50 value less than 200 nM and Ki value less than 100 nM.

IT 613671-14-0 613671-17-3 613671-18-4
613671-19-5 613671-20-8 613671-21-9
613671-24-2 613671-25-3 613671-26-4
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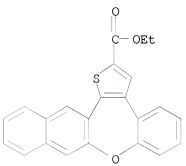
613671-39-9 613671-40-2 613671-41-3
613671-42-4 613671-43-5 613671-44-6
613671-45-7 613671-46-8 861398-65-4
861398-66-5 861398-67-6 861398-68-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzonaphthoazulenes for manufacture of pharmaceutical formulations for treatment and prevention of central nervous system diseases and disorders)

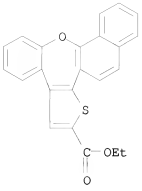
RN 613671-14-0 CAPLUS

CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-carboxylic acid, ethyl ester (CA INDEX NAME)

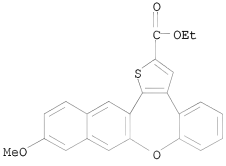


RN 613671-17-3 CAPLUS

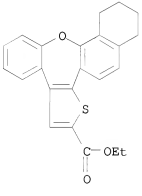
CN Benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-carboxylic acid, ethyl ester (CA INDEX NAME)



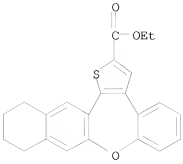
RN 613671-18-4 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-methoxy-, ethyl ester (CA INDEX NAME)



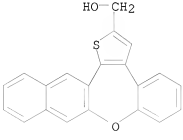
RN 613671-19-5 CAPLUS
CN Benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-carboxylic acid, 1,2,3,4-tetrahydro-, ethyl ester (CA INDEX NAME)



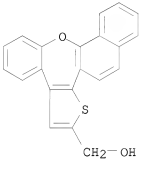
RN 613671-20-8 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-carboxylic acid, 10,11,12,13-tetrahydro-, ethyl ester (CA INDEX NAME)



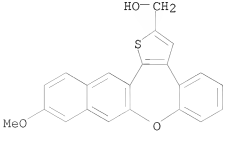
RN 613671-21-9 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-methanol (CA INDEX NAME)



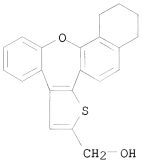
RN 613671-24-2 CAPLUS
CN Benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-methanol (CA INDEX NAME)



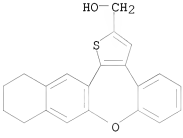
RN 613671-25-3 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-methanol, 11-methoxy- (CA INDEX NAME)



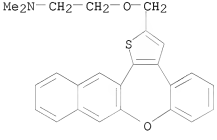
RN 613671-26-4 CAPLUS
CN Benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-methanol, 1,2,3,4-tetrahydro- (CA INDEX NAME)



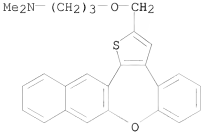
RN 613671-27-5 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-methanol, 10,11,12,13-tetrahydro- (CA INDEX NAME)



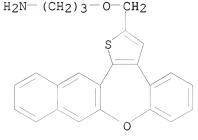
RN 613671-28-6 CAPLUS
CN Ethanamine, 2-(benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)



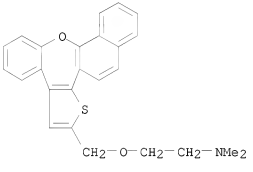
RN 613671-29-7 CAPLUS
CN 1-Propanamine, 3-(benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)



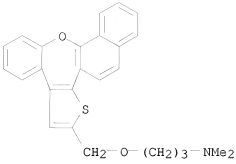
RN 613671-30-0 CAPLUS
CN 1-Propanamine, 3-(benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-ylmethoxy)-
(CA INDEX NAME)



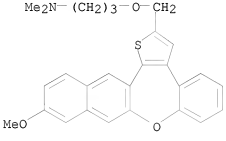
RN 613671-34-4 CAPLUS
CN Ethanamine, 2-(benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-ylmethoxy)-N,N-
dimethyl- (CA INDEX NAME)



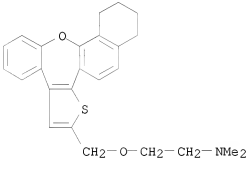
RN 613671-35-5 CAPLUS
CN 1-Propanamine, 3-(benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-ylmethoxy)-
N,N-dimethyl- (CA INDEX NAME)



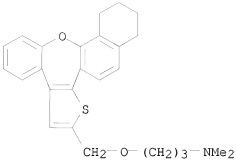
RN 613671-36-6 CAPLUS
CN 1-Propanamine, 3-[(11-methoxybenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



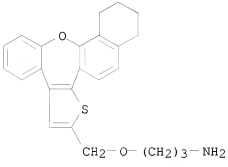
RN 613671-37-7 CAPLUS
CN Ethanamine, N,N-dimethyl-2-[(1,2,3,4-tetrahydrobenzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-yl)methoxy]- (CA INDEX NAME)



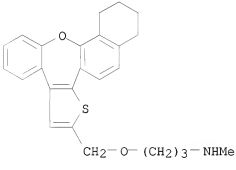
RN 613671-38-8 CAPLUS
CN 1-Propanamine, N,N-dimethyl-3-[(1,2,3,4-tetrahydrobenzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-yl)methoxy]- (CA INDEX NAME)



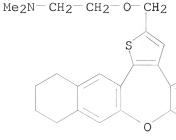
RN 613671-39-9 CAPLUS
CN 1-Propanamine, 3-[(1,2,3,4-tetrahydrobenzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-yl)methoxy]- (CA INDEX NAME)



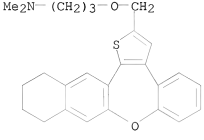
RN 613671-40-2 CAPLUS
CN 1-Propanamine, N-methyl-3-[(1,2,3,4-tetrahydrobenzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-yl)methoxy]- (CA INDEX NAME)



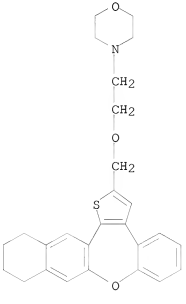
RN 613671-41-3 CAPLUS
CN Ethanamine, N,N-dimethyl-2-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]- (CA INDEX NAME)



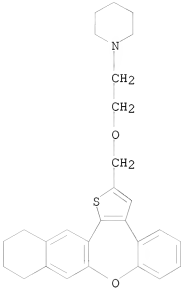
RN 613671-42-4 CAPLUS
CN 1-Propanamine, N,N-dimethyl-3-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]- (CA INDEX NAME)



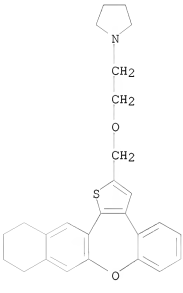
RN 613671-43-5 CAPLUS
CN Morpholine, 4-[2-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



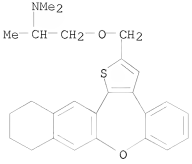
RN 613671-44-6 CAPLUS
CN Piperidine, 1-[2-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



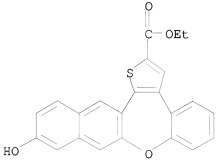
RN 613671-45-7 CAPLUS
CN Pyrrolidine, 1-[2-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



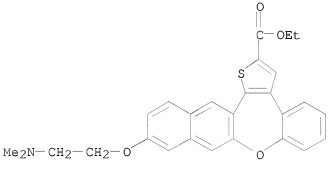
RN 613671-46-8 CAPLUS
CN 2-Propanamine, N,N-dimethyl-1-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]- (CA INDEX NAME)



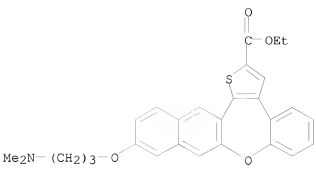
RN 861398-65-4 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-hydroxy-, ethyl ester (CA INDEX NAME)



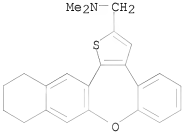
RN 861398-66-5 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-[2-(dimethylamino)ethoxy]-, ethyl ester (CA INDEX NAME)



RN 861398-67-6 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-[3-(dimethylamino)propoxy]-, ethyl ester (CA INDEX NAME)



RN 861398-68-7 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-methanamine, 10,11,12,13-tetrahydro-N,N-dimethyl- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:756722 CAPLUS
DOCUMENT NUMBER: 141:260564
TITLE: Preparation of thiadibenzoazulene derivatives as inhibitors of TNF-α and IL-1 production for the treatment of inflammatory diseases
INVENTOR(S): Mercep, Mladen; Mesic, Milan; Pesic, Dijana; Benko, Iva
PATENT ASSIGNEE(S): Pliva-Istrazivacki Institut D.O.O., Croatia
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

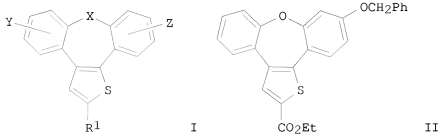
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004078763	A1	20040916	WO 2004-HR5	20040305
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2517847	A1	20040916	CA 2004-2517847	20040305
EP 1603921	A1	20051214	EP 2004-717708	20040305

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK

CN 1768064	A	20060503	CN 2004-80008586			20040305
JP 2006519829	T	20060831	JP 2006-506243			20040305
US 20060069149	A1	20060330	US 2005-221414			20050906
IN 2005CN02550	A	20070831	IN 2005-CN2550			20051005
PRIORITY APPLN. INFO.:			HR 2003-160		A	20030306
			WO 2004-HR5		W	20040305

OTHER SOURCE(S): MARPAT 141:260564

GI



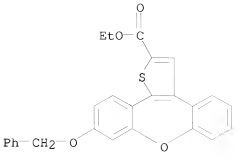
I II

AB Title compds. represented by the formula I [wherein X = O or S; Y, Z = independently O(CH2)mA; A = (un)substituted alkyl, alkenyl, (hetero)aryl, etc.; m = 1-4; R1 = H, halo, (un)substituted alkyl, alkoxy, (hetero)aryl, etc.; and their pharmacol. acceptable esters, salts and solvates thereof] were prepared as inhibitors of tumor necrosis factor-α (TNF-α) and interleukin-1 (IL-1) production For example, reaction of 10-hydroxy-8-oxa-1-thiadibenzo[e,h]azulene-2-carboxylic acid Et ester with benzyl chloride gave II. I were tested for TNF-α and IL-1 secretion in human peripheral blood mononuclear cells with IC50 values of 20 μM or lower, inhibition (30%) of TNF-α production at a dosis of 10 mg/kg and etc. Thus, I and their pharmaceutical compns. are useful as inhibitors of TNF-α and IL-1 production for the treatment of inflammatory diseases inflammatory diseases.

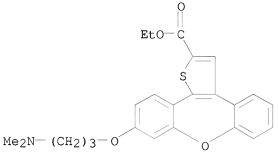
IT 756480-78-1P 756480-79-2P 756480-82-7P
756480-83-8P 756480-85-0P 756480-86-1P
756480-87-2P 756480-88-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of dibenzo[b,f]thieno[2,3-d]oxepins derivs. as inhibitors of TNF-α and IL-1 production for treatment of inflammatory diseases)

RN 756480-78-1 CAPLUS

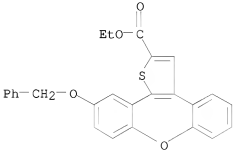
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 10-(phenylmethoxy)-, ethyl ester (CA INDEX NAME)



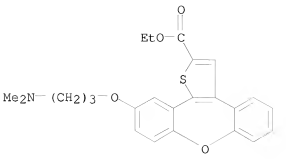
RN 756480-79-2 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid,
10-[3-(dimethylamino)propoxy]-, ethyl ester (CA INDEX NAME)



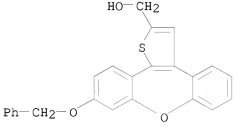
RN 756480-82-7 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-(phenylmethoxy)-,
ethyl ester (CA INDEX NAME)



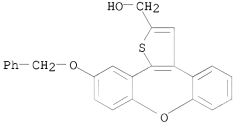
RN 756480-83-8 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid,
11-[3-(dimethylamino)propoxy]-, ethyl ester (CA INDEX NAME)



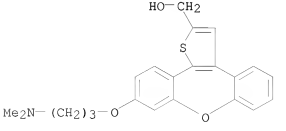
RN 756480-85-0 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-methanol, 10-(phenylmethoxy)- (CA INDEX NAME)



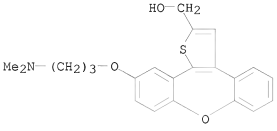
RN 756480-86-1 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-methanol, 11-(phenylmethoxy)- (CA INDEX NAME)



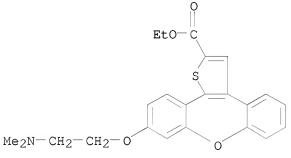
RN 756480-87-2 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-methanol, 10-[3-(dimethylamino)propoxy]- (CA INDEX NAME)



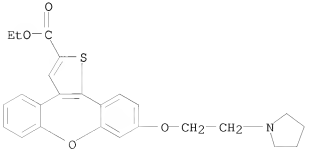
RN 756480-88-3 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-methanol, 11-[3-(dimethylamino)propoxy]-
(CA INDEX NAME)



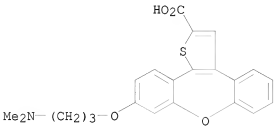
IT 756480-80-5P 756480-81-6P 756480-84-9P
756480-89-4P 756480-90-7P 756480-91-8P
756480-92-9P 756480-93-0P 756480-94-1P
756480-95-2P 756480-96-3P 756480-97-4P
756481-07-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of dibenzo[b,f]thieno[2,3-d]oxepins derivs. as inhibitors of
TNF-α and IL-1 production for treatment of inflammatory diseases)
RN 756480-80-5 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxylic acid,
10-[2-(dimethylamino)ethoxy]-, ethyl ester (CA INDEX NAME)



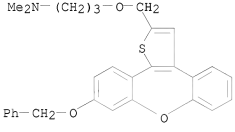
RN 756480-81-6 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid,
10-[2-(1-pyrrolidinyl)ethoxy]-, ethyl ester (CA INDEX NAME)



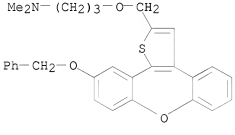
RN 756480-84-9 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxylic acid, 10-[3-(dimethylamino)propoxy]- (CA INDEX NAME)



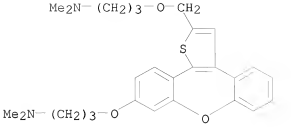
RN 756480-89-4 CAPLUS
CN 1-Propanamine, N,N-dimethyl-3-[[10-(phenylmethoxy)dibenzo[b,f]thieno[3,2-d]oxepin-2-yl]methoxy]- (CA INDEX NAME)



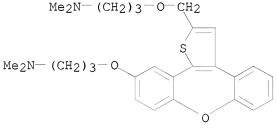
RN 756480-90-7 CAPLUS
CN 1-Propanamine, N,N-dimethyl-3-[[11-(phenylmethoxy)dibenzo[b,f]thieno[3,2-d]oxepin-2-yl]methoxy]- (CA INDEX NAME)



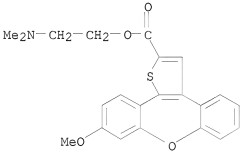
RN 756480-91-8 CAPLUS
CN 1-Propanamine, 3-[[10-[3-(dimethylamino)propoxy]dibenzo[b,f]thieno[2,3-d]oxepin-2-yl]methoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



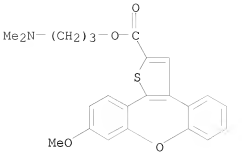
RN 756480-92-9 CAPLUS
CN 1-Propanamine, 3-[[11-[3-(dimethylamino)propoxy]dibenzo[b,f]thieno[2,3-d]oxepin-2-yl]methoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



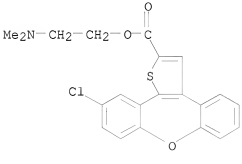
RN 756480-93-0 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxylic acid, 10-methoxy-, 2-(dimethylamino)ethyl ester (CA INDEX NAME)



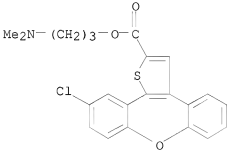
RN 756480-94-1 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxylic acid, 10-methoxy-, 3-(dimethylamino)propyl ester (CA INDEX NAME)



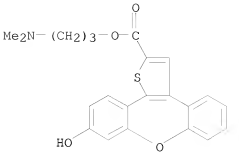
RN 756480-95-2 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxylic acid, 11-chloro-, 2-(dimethylamino)ethyl ester (CA INDEX NAME)



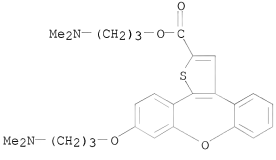
RN 756480-96-3 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-chloro-, 3-(dimethylamino)propyl ester (CA INDEX NAME)



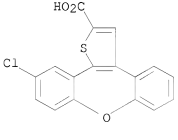
RN 756480-97-4 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxylic acid, 10-hydroxy-, 3-(dimethylamino)propyl ester (CA INDEX NAME)



RN 756481-07-9 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxylic acid, 10-[3-(dimethylamino)propoxy]-, 3-(dimethylamino)propyl ester (CA INDEX NAME)

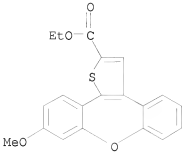


IT 756481-06-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of dibenzo[b,f]thieno[2,3-d]oxepins derivs. as inhibitors of TNF-α and IL-1 production for treatment of inflammatory diseases)
RN 756481-06-8 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-chloro- (CA INDEX NAME)

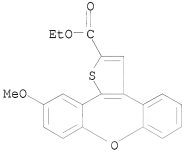


IT 756480-99-6P 756481-00-2P 756481-01-3P
756481-02-4P 756481-03-5P 756481-04-6P
756481-08-0P 756481-09-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of dibenzo[b,f]thieno[2,3-d]oxepins derivs. as inhibitors of TNF-α and IL-1 production for treatment of inflammatory diseases)
RN 756480-99-6 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 10-methoxy-, ethyl

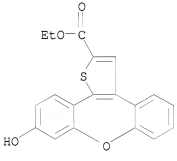
ester (CA INDEX NAME)



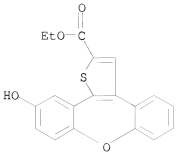
RN 756481-00-2 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-methoxy-, ethyl ester (CA INDEX NAME)



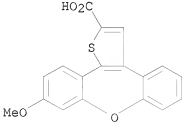
RN 756481-01-3 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxylic acid, 10-hydroxy-, ethyl ester (CA INDEX NAME)



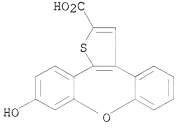
RN 756481-02-4 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-hydroxy-, ethyl ester (CA INDEX NAME)



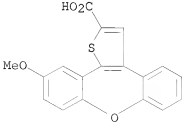
RN 756481-03-5 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 10-methoxy- (CA INDEX NAME)



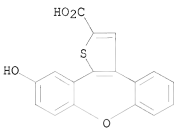
RN 756481-04-6 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxylic acid, 10-hydroxy- (CA INDEX NAME)



RN 756481-08-0 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-methoxy- (CA INDEX NAME)



RN 756481-09-1 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-hydroxy- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:818427 CAPLUS
DOCUMENT NUMBER: 139:323507
TITLE: Preparation of 1- or 3-thienonaphthazulenes as inhibitors of tumor necrosis factor production
INVENTOR(S): Mercep, Mladen; Mesic, Milan; Pesic, Dijana; Ozimec, Ivana; Trojko, Rudolf
PATENT ASSIGNEE(S): Pliva D.D., Croatia
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003084961	A1	20031016	WO 2003-HR14	20030409
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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AU 2003259958	A1	20031020	AU 2003-259958	20030409
EP 1492795	A1	20050105	EP 2003-745847	20030409
EP 1492795	B1	20051116		
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CN 1649876	A	20050803	CN 2003-809957	20030409
JP 2005526827	T	20050908	JP 2003-582158	20030409
AT 310005	T	20051215	AT 2003-745847	20030409
NZ 535622	A	20060331	NZ 2003-535622	20030409
ES 2253694	T3	20060601	ES 2003-745847	20030409
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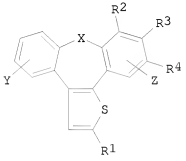
	NO 2004004508	A	20041109	NO 2004-4508		20041021
	IN 2004CN02522	A	20070921	IN 2004-CN2522		20041109
	US 20050137249	A1	20050623	US 2005-510867		20050223
PRIORITY APPLN. INFO.:				HR 2002-303	A	20020410
				WO 2003-HR14	W	20030409

OTHER SOURCE(S): MARPAT 139:323507

GI



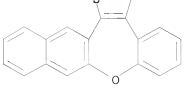
I

AB Thienonaphthazulenes I [X = CH2, O, S, S(O), SO2, NH, protected NH; Y, Z = halogen, alkyl, alkenyl, alkynyl, CF3, haloalkyl, OH, alkoxy, F3CO, acyl, (un)substituted amino, aminoalkyl, SH, alkylthio, alkylsulfinyl, alkylsulfonyl, CO2H, alkoxycarbonyl, NO2; R1 = halogen, (un)substituted alkyl, alkenyl, alkynyl, aryl, heteroaryl, heterocyclic, OH, SH, CO2H, acyl, CONH2, alkylsulfonyl, alkylsulfinyl, NO2; R2R3, R3R4 = (un)substituted CH:CHCH:CH, (CH2)4] were prepared for use as antiinflammatory agents, especially as inhibitors of TNF-α production and interleukin-1 production, as well as analgesics (no data). Thus, I [X = O, Y, Z, R4 = H, R1 = CH2OCH2CH2NMe2, R2R3 = CH:CHCH:CH] was prepared from 2-(2-naphthyloxy)phenylacetic acid, HSCH2CO2Et, and Me2NCH2CH2Cl.HCl.

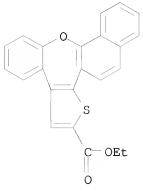
IT 613671-14-0P 613671-17-3P 613671-18-4P
613671-19-5P 613671-20-8P 613671-21-9P
613671-24-2P 613671-25-3P 613671-26-4P
613671-27-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1- or 3-thienonaphthazulenes as inhibitors of tumor necrosis factor production)

RN 613671-14-0 CAPLUS

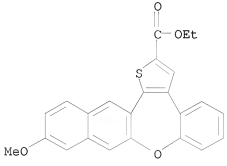
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-carboxylic acid, ethyl ester (CA INDEX NAME)



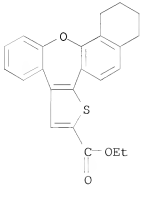
RN 613671-17-3 CAPLUS
CN Benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-carboxylic acid, ethyl ester (CA INDEX NAME)



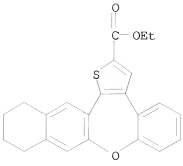
RN 613671-18-4 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-methoxy-, ethyl ester (CA INDEX NAME)



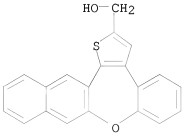
RN 613671-19-5 CAPLUS
CN Benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-carboxylic acid, 1,2,3,4-tetrahydro-, ethyl ester (CA INDEX NAME)



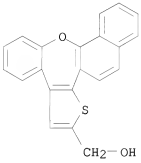
RN 613671-20-8 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-carboxylic acid, 10,11,12,13-tetrahydro-, ethyl ester (CA INDEX NAME)



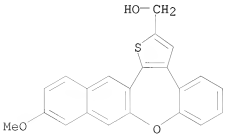
RN 613671-21-9 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-methanol (CA INDEX NAME)



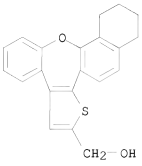
RN 613671-24-2 CAPLUS
CN Benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-methanol (CA INDEX NAME)



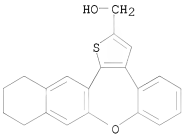
RN 613671-25-3 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-methanol, 11-methoxy- (CA INDEX NAME)



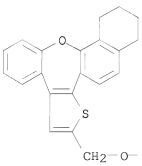
RN 613671-26-4 CAPLUS
CN Benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-methanol, 1,2,3,4-tetrahydro-
(CA INDEX NAME)



RN 613671-27-5 CAPLUS
CN Benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-methanol,
10,11,12,13-tetrahydro- (CA INDEX NAME)



IT 613671-38-8P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
USES (Uses)
(preparation of 1- or 3-thienonaphthazulenes as inhibitors of tumor necrosis
factor production)
RN 613671-38-8 CAPLUS
CN 1-Propanamine, N,N-dimethyl-3-[(1,2,3,4-tetrahydrobenzo[b]naphtho[2,1-
f]thieno[3,2-d]oxepin-8-yl)methoxy]- (CA INDEX NAME)



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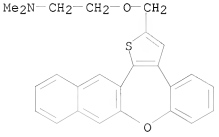
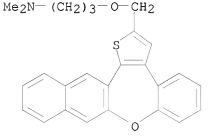
613671-37-7P 613671-39-9P 613671-40-2P

613671-41-3P 613671-42-4P 613671-43-5P
613671-44-6P 613671-45-7P 613671-46-8P
613671-61-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1- or 3-thienonaphthazulenes as inhibitors of tumor necrosis factor production)

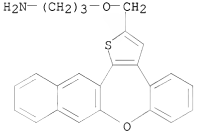
RN 613671-28-6 CAPLUS
CN Ethanamine, 2-(benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)



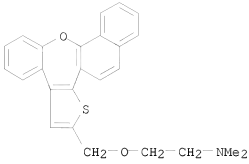
RN 613671-29-7 CAPLUS
CN 1-Propanamine, 3-(benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)



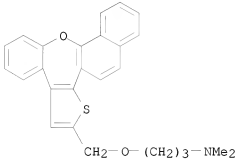
RN 613671-30-0 CAPLUS
CN 1-Propanamine, 3-(benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-ylmethoxy)- (CA INDEX NAME)



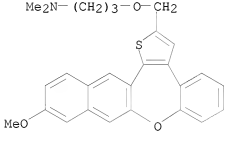
RN 613671-34-4 CAPLUS
CN Ethanamine, 2-(benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)



RN 613671-35-5 CAPLUS
CN 1-Propanamine, 3-(benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)



RN 613671-36-6 CAPLUS
CN 1-Propanamine, 3-[(11-methoxybenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



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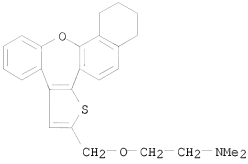
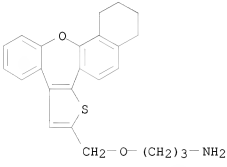
CN Ethanamine, N,N-dimethyl-2-[(1,2,3,4-tetrahydrobenzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-yl)methoxy]- (CA INDEX NAME)



RN 613671-39-9 CAPLUS
CN 1-Propanamine, 3-[(1,2,3,4-tetrahydrobenzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-yl)methoxy]- (CA INDEX NAME)



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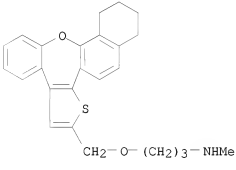
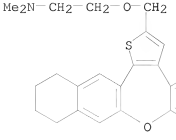
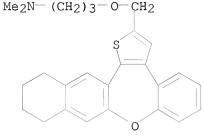
CN 1-Propanamine, N-methyl-3-[(1,2,3,4-tetrahydrobenzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-yl)methoxy]- (CA INDEX NAME)



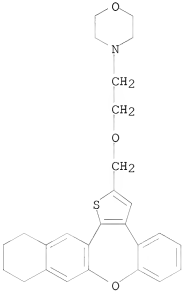
RN 613671-41-3 CAPLUS
CN Ethanamine, N,N-dimethyl-2-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]- (CA INDEX NAME)



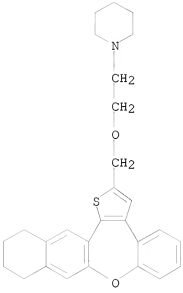
RN 613671-42-4 CAPLUS
CN 1-Propanamine, N,N-dimethyl-3-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]- (CA INDEX NAME)



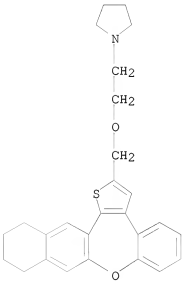
RN 613671-43-5 CAPLUS
CN Morpholine, 4-[2-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



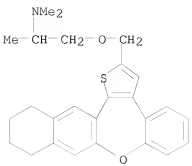
RN 613671-44-6 CAPLUS
CN Piperidine, 1-[2-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



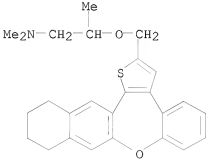
RN 613671-45-7 CAPLUS
CN Pyrrolidine, 1-[2-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



RN 613671-46-8 CAPLUS
CN 2-Propanamine, N,N-dimethyl-1-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]- (CA INDEX NAME)



RN 613671-61-7 CAPLUS
CN 1-Propanamine, N,N-dimethyl-2-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:851165 CAPLUS
DOCUMENT NUMBER: 136:5998
TITLE: Preparation of thienodibenzoazulene compounds as inhibitors of tumor necrosis factor and interleukin production
INVENTOR(S): Mercep, Mladen; Mesic, Milan; Pesic, Dijana; Zupanovic, Zeljko; Hrvacic, Boska
PATENT ASSIGNEE(S): Pliva, Farmaceutska Industrija, Dionicko Drustvo, Croatia
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087890	A1	20011122	WO 2001-HR27	20010516
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

HR	2000000310	A1	20020228	HR 2000-310	20000517
CA	2409090	A1	20011122	CA 2001-2409090	20010516
AU	2001056560	A	20011126	AU 2001-56560	20010516
EP	1284977	A1	20030226	EP 2001-929882	20010516
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BR	2001011202	A	20030401	BR 2001-11202	20010516
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HU	2003002295	A3	20070328		
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NO	2002005510	A	20030114	NO 2002-5510	20021115
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IN	2002CN02041	A	20050225	IN 2002-CN2041	20021211
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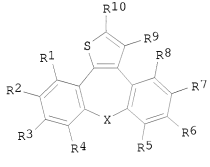
PRIORITY APPLN. INFO.:

HR 2000-310	A	20000517
WO 2001-HR27	W	20010516
US 2002-298217	A1	20021118

OTHER SOURCE(S): CASREACT 136:5998; MARPAT 136:5998

GI



I

AB The title compds. [I; X = CH2, a heteroatom such as O, S, S(O), S(O)2 or NR13(wherein R13 = H, C1-6 alkyl, C1-6 alkylcarbonyl, arylcarbonyl, C1-6 alkylsulfonyl, arylsulfonyl); R1, R2, R3, R4, R5, R6, R7, R5, R9 = H, halogens (fluorine, chlorine or bromine), C1-7 alkyl, alkenyl, aryl, heteroaryl; or they can represent different groups : halomethyl, hydroxy, C1-7 alkoxy or aryloxy, C1-7 alkylthio or arylthio, C1-7 alkylsulfonyl, cyano, amino, mono- and di(C1-7 substituted) amines, derivs. of carboxylic group (C1-C7 carboxylic acids and their anhydrides, C1-7 unsubstituted or mono- or disubstituted amides, C1-7 alkyl or aryl esters), C1-7 derivs. of carbonyl group (C1-7 alkyl or arylcarbonyls); R10 = C2-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, aryl or heteroaryl, C1-15 haloalkyl, C1-15 hydroxyalkyl, C1-15 alkoxy, C1-15 alkylthio, C3-15 alkylcarbonyl, C2-15 alkylcarboxylic acid, C2-15 alkyl ester, C1-15 alkylsulfonyl, C1-15 alkylarylsulfonyl, arylsulfonyl, C1-15 alkylamines represented by the general formula -(CH2)n-A (wherein n means 1-15, and one or more methylene

groups that can be substituted with an oxygen or sulfur atom, and A represents a five- or six-membered, saturated or unsatd. ring with one, two or three heteroatoms, or -NR11R12; wherein R11 and R12 independently from each other represent hydrogen, C1-7 alkyl, alkenyl, alkynyl, aryl or heteroaryl, or a heterocycle with 1-3 heteroatoms)] are prepared These compds. I are inhibitors of the production of cytokines or inflammation mediators, e.g. tumor necrosis factor alpha (TNF-α) and interleukin 1 (IL-1), and useful for the treatment or prophylaxis of any pathol. conditions or diseases induced by excessive unregulated production of cytokines or inflammation mediators. They also demonstrate an analgetic action and can be used to relieve pain and thereby useful as anti-inflammatory agents, inhibitors of TNF-α and IL-1 secretion, or analgesics. Thus, 0.1 g benzyltriethylammonium chloride and a toluene solution of 0.28 g 2-(hydroxymethyl)-8-oxa-1-thia-dibenzo[e,h]azulene were added to a solution of 2.2 g 3-dimethylaminopropyl chloride hydrochloride in 5 mL 50% aqueous NaOH and the resulting mixture was refluxed for 4 h with vigorous stirring to give dimethyl-[3-(8-oxa-1-thia-dibenzo[e,h]azulen-2-ylmethoxy)propyl]amine (II). II.HCl and 3 other I demonstrated activity in at least two of investigated biol. tests such as TNF-α and IL-1 secretion in mononuclear cells of human peripheral blood or mouse peritoneal macrophages in vitro, LPS-induced excessive secretion of TNF-α or IL-1 in mice, writhing test for analgesic activity in mice, and LPS-induced shock in mice (no detailed data given).

IT 374799-32-3P, Dimethyl-[3-[8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]propyl]amine hydrochloride 374799-34-5P, Dimethyl-[3-[8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]propyl]amine 374799-37-8P, Dimethyl-[2-[8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]amine hydrochloride 374799-39-0P, Dimethyl-[2-[8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]amine 374799-41-4P, 4-[2-[8-Oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]morpholine hydrochloride 374799-44-7P, 4-[2-[8-Oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]morpholine 374799-47-0P, 1-[2-[8-Oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]piperidine hydrochloride 374799-49-2P, 1-[2-[8-Oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]piperidine 374799-51-6P, 1-[2-[8-Oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]pyrrolidine hydrochloride 374799-54-9P, 1-[2-[8-Oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]pyrrolidine 374799-56-1P, [3-[9-Chloro-8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]propyl]dimethylamine 374799-59-4P, [2-[9-Chloro-8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]dimethylamine 374799-62-9P, 4-[2-[9-Chloro-8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]morpholine 374799-64-1P, 1-[2-[9-Chloro-8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]piperidine 374799-66-3P, 1-[2-[9-Chloro-8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]pyrrolidine 374799-68-5P, [3-[11-Chloro-8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]propyl]dimethylamine 374799-70-9P, [2-[11-Chloro-8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]dimethylamine 374799-72-1P, 4-[2-[11-Chloro-8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]morpholine 374799-74-3P, 1-[2-[11-Chloro-8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]piperidine 374799-76-5P, 1-[2-[11-Chloro-8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]pyrrolidine 374799-79-8P 374799-81-2P 374799-83-4P, [2-[11-Fluoro-8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]dimethylamine hydrochloride 374799-85-6P, [2-[11-Fluoro-8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]ethyl]dimethylamine 374799-87-8P, 4-[2-[11-Fluoro-8-oxa-1-thiadibenzo[e,h]azulen-2-

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374801-08-8P, 3-[11-Chloro-8-oxa-1-thiadibenzo[e,h]azulen-2-
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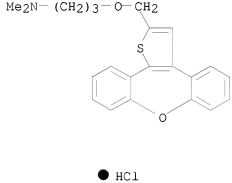
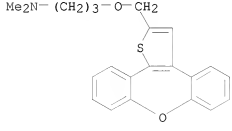
374801-10-2P, 4-[11-Chloro-8-oxa-1-thiadibenzo[e,h]azulen-2-yl]but-
3-ene-2-one 374801-12-4P 374801-13-5P,
3-[11-Fluoro-8-oxa-1-thiadibenzo[e,h]azulen-2-yl]propionic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of thienodibenzoazulene compds. as tumor necrosis factor and
interleukin production inhibitors, antiinflammatory agents, and analgesics)

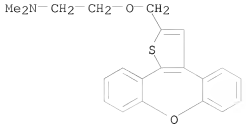
RN 374799-32-3 CAPLUS
CN 1-Propanamine, 3-(dibenzo[b,f]thieno[2,3-d]oxepin-2-ylmethoxy)-N,N-
dimethyl-, hydrochloride (1:1) (CA INDEX NAME)



RN 374799-34-5 CAPLUS
CN 1-Propanamine, 3-(dibenzo[b,f]thieno[2,3-d]oxepin-2-ylmethoxy)-N,N-
dimethyl- (CA INDEX NAME)

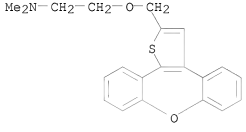


RN 374799-37-8 CAPLUS
CN Ethanamine, 2-(dibenzo[b,f]thieno[2,3-d]oxepin-2-ylmethoxy)-N,N-dimethyl-,
hydrochloride (1:1) (CA INDEX NAME)

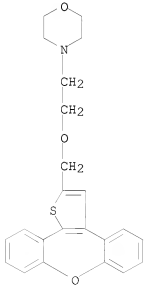


● HCl

RN 374799-39-0 CAPLUS
CN Ethanamine, 2-(dibenzo[b,f]thieno[2,3-d]oxepin-2-ylmethoxy)-N,N-dimethyl-
(CA INDEX NAME)



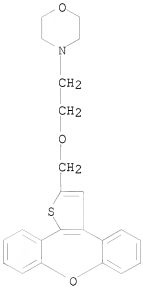
RN 374799-41-4 CAPLUS
CN Morpholine, 4-[2-(dibenzo[b,f]thieno[3,2-d]oxepin-2-ylmethoxy)ethyl]-,
hydrochloride (1:1) (CA INDEX NAME)



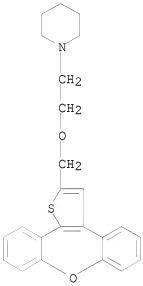
● HCl

RN 374799-44-7 CAPLUS
CN Morpholine, 4-[2-(dibenzo[b,f]thieno[3,2-d]oxepin-2-ylmethoxy)ethyl]- (CA

INDEX NAME)

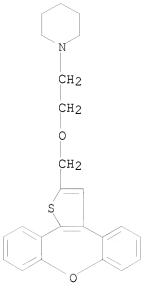


RN 374799-47-0 CAPLUS
CN Piperidine, 1-[2-(dibenzo[b,f]thieno[3,2-d]oxepin-2-ylmethoxy)ethyl]-, hydrochloride (1:1) (CA INDEX NAME)

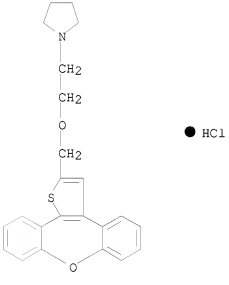


● HCl

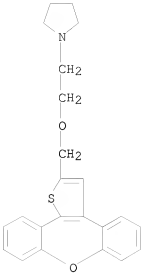
RN 374799-49-2 CAPLUS
CN Piperidine, 1-[2-(dibenzo[b,f]thieno[3,2-d]oxepin-2-ylmethoxy)ethyl]- (CA INDEX NAME)



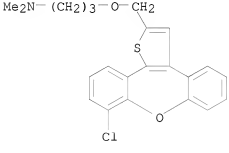
RN 374799-51-6 CAPLUS
CN Pyrrolidine, 1-[2-(dibenzo[b,f]thieno[3,2-d]oxepin-2-ylmethoxy)ethyl]-, hydrochloride (1:1) (CA INDEX NAME)



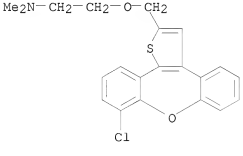
RN 374799-54-9 CAPLUS
CN Pyrrolidine, 1-[2-(dibenzo[b,f]thieno[3,2-d]oxepin-2-ylmethoxy)ethyl]- (CA INDEX NAME)



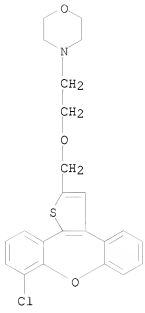
RN 374799-56-1 CAPLUS
CN 1-Propanamine, 3-[(9-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



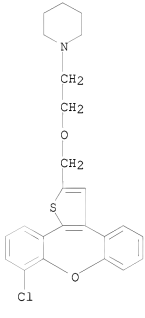
RN 374799-59-4 CAPLUS
CN Ethanamine, 2-[(9-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



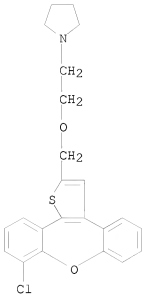
RN 374799-62-9 CAPLUS
CN Morpholine, 4-[2-[(9-chlorodibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



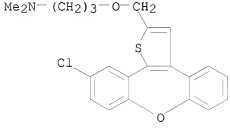
RN 374799-64-1 CAPLUS
CN Piperidine, 1-[2-[(9-chlorodibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



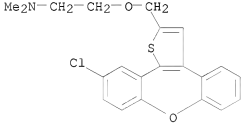
RN 374799-66-3 CAPLUS
CN Pyrrolidine, 1-[2-[(9-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



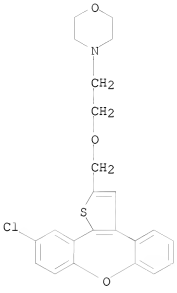
RN 374799-68-5 CAPLUS
CN 1-Propanamine, 3-[(11-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



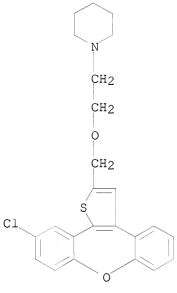
RN 374799-70-9 CAPLUS
CN Ethanamine, 2-[(11-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



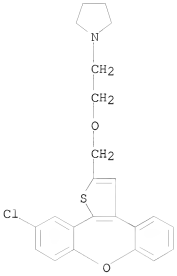
RN 374799-72-1 CAPLUS
CN Morpholine, 4-[2-[(11-chlorodibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



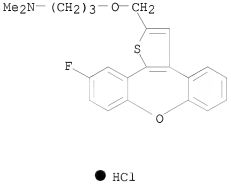
RN 374799-74-3 CAPLUS
CN Piperidine, 1-[2-[(11-chlorodibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



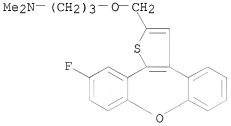
RN 374799-76-5 CAPLUS
CN Pyrrolidine, 1-[2-[(11-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



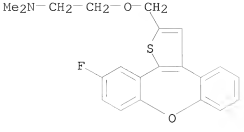
RN 374799-79-8 CAPLUS
CN 1-Propanamine, 3-[(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl-, hydrochloride (1:1) (CA INDEX NAME)



RN 374799-81-2 CAPLUS
CN 1-Propanamine, 3-[(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)

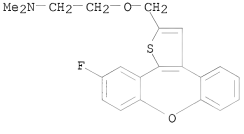


RN 374799-83-4 CAPLUS
CN Ethanamine, 2-[(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl-, hydrochloride (1:1) (CA INDEX NAME)

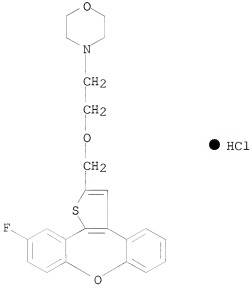


● HCl

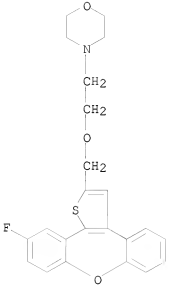
RN 374799-85-6 CAPLUS
CN Ethanamine, 2-[(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



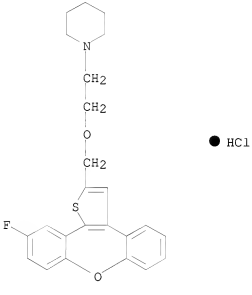
RN 374799-87-8 CAPLUS
CN Morpholine, 4-[2-[(11-fluorodibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]-, hydrochloride (1:1) (CA INDEX NAME)



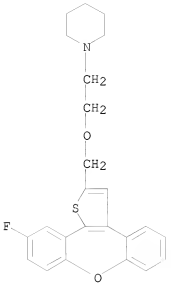
RN 374799-89-0 CAPLUS
CN Morpholine, 4-[2-[(11-fluorodibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



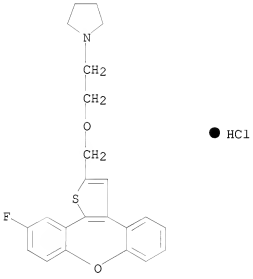
RN 374799-91-4 CAPLUS
CN Piperidine, 1-[2-[(11-fluorodibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]-, hydrochloride (1:1) (CA INDEX NAME)



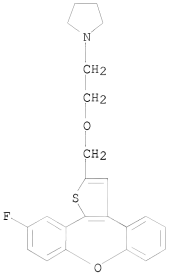
RN 374799-94-7 CAPLUS
CN Piperidine, 1-[2-[(11-fluorodibenzo[b,f]thieno[3,2-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



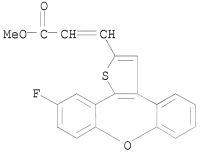
RN 374799-96-9 CAPLUS
CN Pyrrolidine, 1-[2-[(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]ethyl]-, hydrochloride (1:1) (CA INDEX NAME)



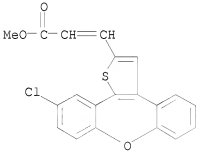
RN 374799-98-1 CAPLUS
CN Pyrrolidine, 1-[2-[(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]ethyl]- (CA INDEX NAME)



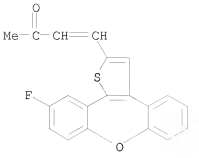
RN 374801-07-7 CAPLUS
CN 2-Propenoic acid, 3-(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)-, methyl ester (CA INDEX NAME)



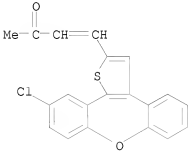
RN 374801-08-8 CAPLUS
CN 2-Propenoic acid, 3-(11-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)-, methyl ester (CA INDEX NAME)



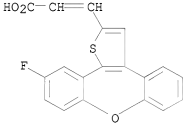
RN 374801-09-9 CAPLUS
CN 3-Buten-2-one, 4-(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)- (CA INDEX NAME)



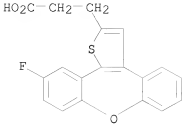
RN 374801-10-2 CAPLUS
CN 3-Buten-2-one, 4-(11-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)- (CA INDEX NAME)



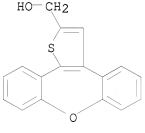
RN 374801-12-4 CAPLUS
CN 2-Propenoic acid, 3-(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)- (CA INDEX NAME)



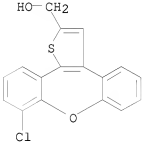
RN 374801-13-5 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-propanoic acid, 11-fluoro- (CA INDEX NAME)



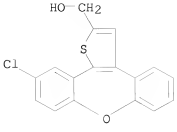
IT 374801-15-7P, 8-Oxa-1-thiadibenzo[e,h]azulen-2-ylmethanol
374801-16-8P 374801-17-9P 374801-18-0P
374801-37-3P 374801-40-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of thienodibenzoazulene compds. as tumor necrosis factor and interleukin production inhibitors, antiinflammatory agents, and analgesics)
RN 374801-15-7 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-methanol (CA INDEX NAME)



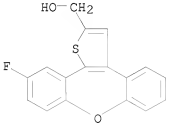
RN 374801-16-8 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-methanol, 9-chloro- (CA INDEX NAME)



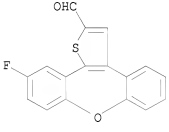
RN 374801-17-9 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-methanol, 11-chloro- (CA INDEX NAME)



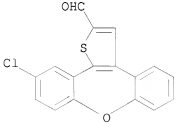
RN 374801-18-0 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-methanol, 11-fluoro- (CA INDEX NAME)



RN 374801-37-3 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxaldehyde, 11-fluoro- (CA INDEX NAME)



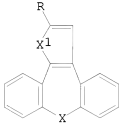
RN 374801-40-8 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxaldehyde, 11-chloro- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1977:171292 CAPLUS
DOCUMENT NUMBER: 86:171292
ORIGINAL REFERENCE NO.: 86:26901a,26904a
TITLE: Study of the Vilsmeier-Haack reaction of tricyclic ketones: 10,11-dihydro-10-oxo-5H-dibenzo[a,d]cycloheptene, 10,11-dihydro-10-oxodibenzo[b,f]oxepin and 10,11-dihydro-10-oxodibenzo[b,f]thiepin. Synthesis of new heterotetracyclic compounds
AUTHOR(S): Cagniant, Paul; Kirsch, Gilbert
CORPORATE SOURCE: Lab. Chim. Org., Univ. Metz, Metz, Fr.
SOURCE: Comptes Rendus des Seances de l'Academie des Sciences, Serie C: Sciences Chimiques (1976), 283(15), 683-6
CODEN: CHDCAQ; ISSN: 0567-6541
DOCUMENT TYPE: Journal
LANGUAGE: French
GI



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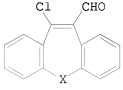


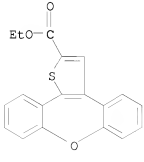
II

AB Condensed heterocycles I (X = CH2, O, S, X1 = S, R = H; X = O, X1 = Se, R = H) were prepared by treating 2-PhXC6H4CH2Cl with NaCN, hydrolyzing 2-PhXC6H4CH2CN, cyclizing 2-PhXC6H4CH2CO2H, chloroformylating the resulting ketones, cyclizing II with BrCH2CO2Et and Na2S or Na2Se, and decarboxylating I (R = CO2Et). I (R = Me) was similarly prepared with BrCHMeCO2Et.

IT 62551-05-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and decarboxylation of)

RN 62551-05-7 CAPLUS

CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxylic acid, ethyl ester (CA INDEX NAME)



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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                    52.23     238.31

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -7.38      -7.38

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DICTIONARY FILE UPDATES:  30 DEC 2008  HIGHEST RN 1092172-37-6

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http://www.cas.org/support/stngen/stndoc/properties.html

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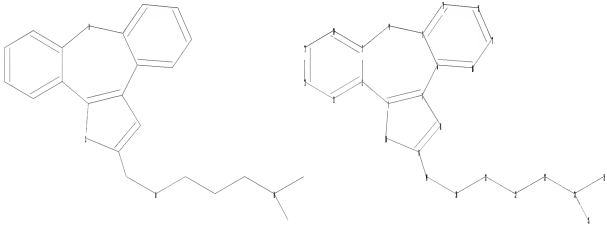

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chain nodes :
19  20  21  22  23  24  25  26
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18
chain bonds :
```

9-19 19-20 20-21 21-22 22-23 23-24 24-25 24-26
ring bonds :
1-2 1-7 1-10 2-3 2-11 3-4 3-14 4-5 5-6 5-15 6-7 6-18 7-8 8-9 9-10
11-12 12-13 13-14 15-16 16-17 17-18
exact/norm bonds :
1-2 1-7 1-10 3-4 4-5 6-7 7-8 8-9 9-10 19-20 20-21 23-24 24-25 24-26
exact bonds :
9-19 21-22 22-23
normalized bonds :
2-3 2-11 3-14 5-6 5-15 6-18 11-12 12-13 13-14 15-16 16-17 17-18

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS

L5 STRUCTURE UPLOADED

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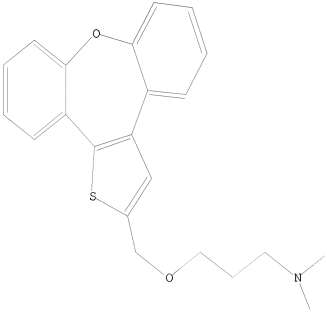

Structure attributes must be viewed using STN Express query preparation.

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FULL SUBSET SEARCH INITIATED 12:22:14 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED - 44 TO ITERATE

100.0% PROCESSED 44 ITERATIONS 20 ANSWERS
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L6            20 SEA SUB=L3 SSS FUL L5

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                     0.00      -7.38

FILE 'CAPLUS' ENTERED AT 12:22:19 ON 31 DEC 2008
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FILE COVERS 1907 - 31 Dec 2008  VOL 150 ISS 1
FILE LAST UPDATED: 30 Dec 2008  (20081230/ED)

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reclassification data for the third quarter of 2008.

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YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:n


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L7             6 L6

=> d l7 1-6 ibib abs hitstr

L7   ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2008:493006  CAPLUS
DOCUMENT NUMBER:          148:472014
TITLE:                    Thienodibenzoazulene compounds as tumor necrosis
                          factor inhibitors and their preparation,
                          pharmaceutical compositions and use in the treatment
                          of inflammation
INVENTOR(S):              Mercep, Mladen; Mesic, Milan; Pesic, Dijana;
                          Zupanovic, Zeljko; Hrvacic, Boska
PATENT ASSIGNEE(S):       Pliva Farmaceutska Industrija, Dionicko Drustvo,
                          Croatia
SOURCE:                   U.S. Pat. Appl. Publ., 23pp., Cont.-in-part of Appl.
                          No. PCT/HR2001/00027.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
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LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030153750	A1	20030814	US 2002-298217	20021118
US 6897211	B2	20050524		
HR 2000000310	A1	20020228	HR 2000-310	20000517
WO 2001087890	A1	20011122	WO 2001-HR27	20010516
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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US 20050171091	A1	20050804	US 2005-90743	20050325
PRIORITY APPLN. INFO.:			HR 2000-310	A 20000517
			WO 2001-HR27	A2 20010516
			US 2002-298217	A1 20021118

OTHER SOURCE(S): CASREACT 148:472014; MARPAT 148:472014
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to the dibenzoazulene compds. of formula I as well as to their pharmaceutical prepns. for the inhibition of tumor necrosis factor alpha (TNF-α) and interleukine 1 (IL-1) in mammal at all diseases and conditions where these mediators are excessively secreted. The compds. of the invention also demonstrate an analgetic action and can be used to relieve pain. Compds. of formula I wherein X is CH2, O, SO0-2 and NH and derivs.; R1-R9 are independently H, halo, C1-7 alkyl, alkenyl, (hetero)aryl, OH, C1-7 alkoxy, etc.; R10 is C2-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, (hetero)aryl, C1-15 haloalkyl, etc.; and their pharmaceutically acceptable salts and solvates thereof, are claimed. Example compound II•HCl was prepared by O-alkylation of 3-(8-oxa-1-thiadibenzo[e,h]azulene)methanol with 3-dimethylaminopropyl chloride. All the invention compds. were evaluated for their TNF-α inhibitory activity (some data given).

IT 374799-68-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of thienodibenzoazulene compds. as TNF inhibitors useful in the treatment of inflammation)

RN 374799-68-5 CAPLUS

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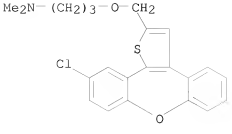

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1019856-16-6P
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(drug candidate; preparation of thienodibenzoazulene compds. as TNF inhibitors useful in the treatment of inflammation)
RN 374799-32-3 CAPLUS
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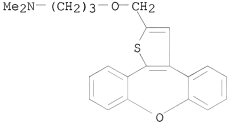

● HCl

RN 374799-56-1 CAPLUS
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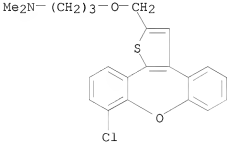

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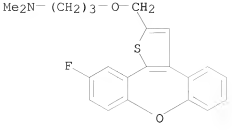

● HCl

RN 1019856-16-6 CAPLUS
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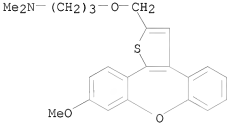

IT 374799-34-5P 374799-81-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of thienodibenzoazulene compds. as TNF inhibitors useful in the treatment of inflammation)
RN 374799-34-5 CAPLUS
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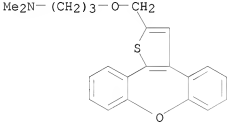

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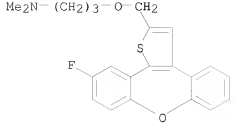

L7 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:959196 CAPLUS
DOCUMENT NUMBER: 147:322957
TITLE: Preparation of 1- or 3-thia-benzonaphthoazulenes as inhibitors of tumor necrosis factor production and intermediates for the preparation thereof
INVENTOR(S): Mercep, Mladen; Mesic, Milan; Pesic, Dijana; Ozimec, Ivana; Trojko, Rudolf
PATENT ASSIGNEE(S): Glaxosmith Kline Istrazivocki Centar Zagreb, D.O.O., Croatia
SOURCE: U.S., 18pp., Cont.-in-part of Appl. No. PCT/HR03/00014.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 7262309	B2	20070828	US 2004-963979	20041012
US 20050130964	A1	20050616		
HR 2002000303	B1	20070531	HR 2002-303	20020410
WO 2003084961	A1	20031016	WO 2003-HR14	20030409

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: HR 2002-303 A 20020410
WO 2003-HR14 A2 20030409

OTHER SOURCE(S): MARPAT 147:322957
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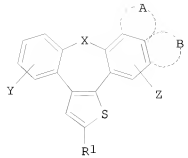

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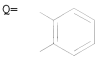

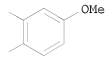

AB The present invention relates to benzonaphthoazulene derivs. of thiophene class [I; X = CH2, O, S, S(:O), S(:O)2, or (un)protected NH; Y, Z = H, halogen, C1-4 alkyl, C2-4 alkenyl, C2-4 alkynyl, CF3, halo-C1-4 alkyl, HO, C1-4 alkoxy, CF3O, C1-4 alkanoyl, NH2, amino-C1-4 alkyl, C1-4 alkylamino, N-(C1-4 alkyl)amino, N,N-di(C1-4 alkyl)amino, SH, C1-4 alkylthio, C1-4 alkylsulfonyl, C1-4 alkylsulfinyl, CO2H, C1-4 alkoxycarbonyl, NO2; one of the ring A and B is present while is the other one is absent, and is selected from the group consisting of Q, Q1, and Q2; R1 = (un)substituted C1-7 alkyl, C1-7 alkyloxycarbonyl, (CH2)m-Q3-(CH2)n-Q4-NR2R3; wherein R2, R3 = H, C1-4 alkyl, or aryl or NR2R3 taken together forms (un)substituted heterocyclyl or heteroaryl; n = an integer of 0-3; m = an integer of 1-3; Q3, Q4 = O, S, C(yl)(y2), N(yl), C(yl):CH, C.tplbond.C; yl, y2 = H, halogen, HO, C1-4 alkoxy, C1-4 alkanoyl, SH, C1-4 alkylthio, C1-4 alkylsulfonyl, C1-4 alkylsulfinyl, NO2, etc.; or yl and y2 taken together with the carbon atom to which they are attached form carbonyl or imino group] and their pharmacol. acceptable salts and solvates. These compds. inhibit the production of tumor necrosis factor-α (TNF-α) and interleukin-1 (IL-1), possess antiinflammatory or analgetic effects, and are useful for treating inflammation associated with TNF-α, in particular rheumatoid arthritis. Thus, Et 2-mercaptoacetate (0.005 mol) and triethylamine (1.0 mL) were added to a solution of 12-chloro-5-oxabenzo[4,5]cyclohepta[1,2-b]naphthalene-13-carboxaldehyde (0.005 mol) in 10 mL pyridine and the mixture was refluxed under stirring for 3 h to give 8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulene-2-carboxylic acid Et ester as a white solid. Two compds., namely dimethyl[2-(8-oxa-1-thiabenzo[e]naphtho[1,2-h]azulen-2-ylmethoxy)ethyl]amine and dimethyl[3-(11-methoxy-8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulen-2-ylmethoxy)propyl]amine, showed activity in at least two investigated assays selected from (1) inhibitory action on TNF-α and IL-1 secretion in human peripheral blood mononuclear cells or mouse peritoneal macrophages, resp., in vitro, (2) inhibitory action on LPS-induced excessive TNF-α or IL-1 secretion in mice, (3) writhing assay for analgetic activity in mice, and (4) LPS-induced shock in mice.

IT 613671-29-7P, Dimethyl[3-[(8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulen-2-yl)methoxy]propyl]amine 613671-35-5P, Dimethyl[3-[(8-oxa-1-thiabenzo[e]naphtho[1,2-h]azulen-2-yl)methoxy]propyl]amine 613671-36-6P, Dimethyl[3-[(11-methoxy-8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulen-2-yl)methoxy]propyl]amine 613671-38-8P, Dimethyl[3-[(9,10,11,12-tetrahydro-8-oxa-1-thiabenzo[e]naphtho[1,2-h]azulen-2-yl)methoxy]propyl]amine 613671-42-4P,

Dimethyl[3-[(10,11,12,13-tetrahydro-8-oxa-1-thiabenzo[e]naphtho[3,2-h]azulen-2-yl)methoxy]propyl]amine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1- or 3-thia-benzonaphthoazulenes as inhibitors of tumor necrosis factor production for treating inflammation and rheumatoid arthritis)

RN 613671-29-7 CAPLUS
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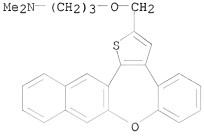

RN 613671-35-5 CAPLUS
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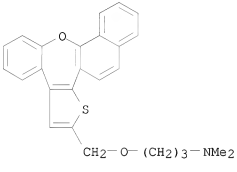
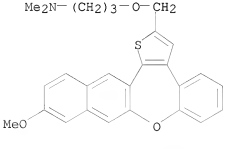


RN 613671-36-6 CAPLUS
CN 1-Propanamine, 3-[(11-methoxybenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



RN 613671-38-8 CAPLUS
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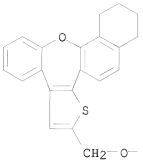

RN 613671-42-4 CAPLUS
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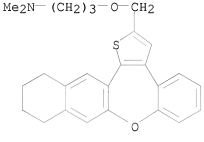

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:729528 CAPLUS
DOCUMENT NUMBER: 143:179664
TITLE: Benzonaphthoazulenes for the manufacture of pharmaceutical formulations for the treatment and prevention of central nervous system diseases and disorders
INVENTOR(S): Mercep, Mladen; Mesic, Milan; Pesic, Dijana; Ozimeclandek, Ivana; Trojko, Rudolf; Rupcic, Renata
PATENT ASSIGNEE(S): Pliva-Istrazivacki Institut D.O.O., Croatia
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005072728	A1	20050811	WO 2005-HR8	20050127
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CN 1938016	A	20070328	CN 2005-80010392		20050127
JP 2007519698	T	20070719	JP 2006-550310		20050127
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PRIORITY APPLN. INFO.:			HR 2004-104	A	20040130
			WO 2005-HR8	W	20050127

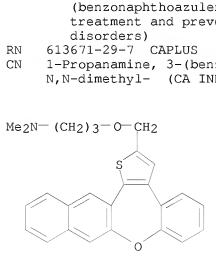
OTHER SOURCE(S): MARPAT 143:179664

AB The present invention relates to the use of compds. from the group of benzonaphthoazenes and of their pharmaceutically acceptable salts and solvates for the manufacture of a pharmaceutical formulation for the treatment and prevention of diseases, damages and disorders of the central nervous system (CNS) caused by disorders of the neurochem. equilibrium of biogenic amines or other transmitters. Thus, in vitro affinity of benzonaphthoazulenes for binding to recombinant human 5-HT2A and 5-HT2C serotonin receptors expressed in CHO-K1 or COS-7 cells was determined using a radioligand. The radioligand binding was inhibited by the test compds. proportionally to the affinity of a certain compound for the receptor and to the concentration of the compound Compds. showing IC50 and Ki in concns. lower than 1 μM were considered to be active. Compound dimethyl-[3-(1,8-dithia-benzo[e]naphtho[3,2-h]azulen-2-ylmethoxy)-propyl]-amine and dimethyl-[3-(3, 10-dithia-benzo[e]naphtho[1,2-h]azulen-2-ylmethoxy)-propyl]-amine showed binding affinity to 5-HT2A and 5-HT2C serotonin receptors expressed as IC50 value less than 200 nM and Ki value less than 100 nM.

IT 613671-29-7 613671-35-5 613671-36-6
613671-38-8 613671-42-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzonaphthoazulenes for manufacture of pharmaceutical formulations for treatment and prevention of central nervous system diseases and disorders)

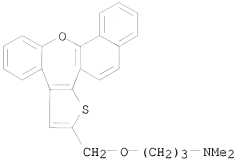
RN 613671-29-7 CAPLUS

CN 1-Propanamine, 3-(benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)

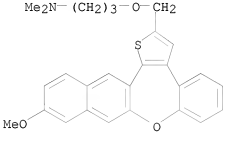


RN 613671-35-5 CAPLUS

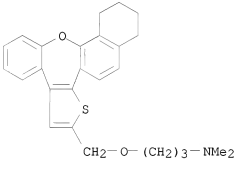
CN 1-Propanamine, 3-(benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)



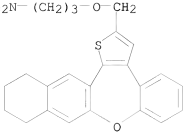
RN 613671-36-6 CAPLUS
CN 1-Propanamine, 3-[(11-methoxybenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



RN 613671-38-8 CAPLUS
CN 1-Propanamine, N,N-dimethyl-3-[(1,2,3,4-tetrahydrobenzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-yl)methoxy]- (CA INDEX NAME)



RN 613671-42-4 CAPLUS
CN 1-Propanamine, N,N-dimethyl-3-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]- (CA INDEX NAME)



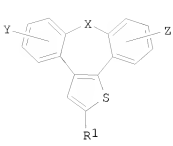
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:756722 CAPLUS
DOCUMENT NUMBER: 141:260564
TITLE: Preparation of thiadibenzoazulene derivatives as inhibitors of TNF-α and IL-1 production for the treatment of inflammatory diseases
INVENTOR(S): Mercep, Mladen; Mesic, Milan; Pesic, Dijana; Benko, Iva
PATENT ASSIGNEE(S): Pliva-Istrazivacki Institut D.O.O., Croatia
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004078763	A1	20040916	WO 2004-HR5	20040305
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2517847	A1	20040916	CA 2004-2517847	20040305
EP 1603921	A1	20051214	EP 2004-717708	20040305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
CN 1768064	A	20060503	CN 2004-80008586	20040305
JP 2006519829	T	20060831	JP 2006-506243	20040305
US 20060069149	A1	20060330	US 2005-221414	20050906
IN 2005CN02550	A	20070831	IN 2005-CN2550	20051005

PRIORITY APPLN. INFO.: HR 2003-160 A 20030306
WO 2004-HR5 W 20040305

OTHER SOURCE(S): MARPAT 141:260564
GI



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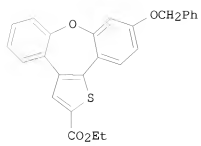


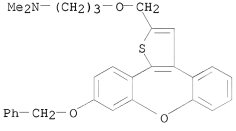
II

AB Title compds. represented by the formula I [wherein X = O or S; Y, Z = independently O(CH2)mA; A = (un)substituted alkyl, alkenyl, (hetero)aryl, etc.; m = 1-4; R1 = H, halo, (un)substituted alkyl, alkoxy, (hetero)aryl, etc.; and their pharmacol. acceptable esters, salts and solvates thereof] were prepared as inhibitors of tumor necrosis factor-α (TNF-α) and interleukin-1 (IL-1) production For example, reaction of 10-hydroxy-8-oxa-1-thiadibenzo[e,h]azulene-2-carboxylic acid Et ester with benzyl chloride gave II. I were tested for TNF-α and IL-1 secretion in human peripheral blood mononuclear cells with IC50 values of 20 μM or lower, inhibition (30%) of TNF-α production at a dosis of 10 mg/kg and etc. Thus, I and their pharmaceutical compns. are useful as inhibitors of TNF-α and IL-1 production for the treatment of inflammatory diseases inflammatory diseases.

IT 756480-89-4P 756480-90-7P 756480-91-8P
756480-92-9P 756480-94-1P 756480-96-3P
756480-97-4P 756481-07-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dibenzo[b,f]thieno[2,3-d]oxepins derivs. as inhibitors of TNF-α and IL-1 production for treatment of inflammatory diseases)

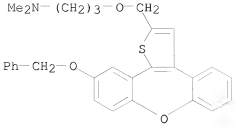
RN 756480-89-4 CAPLUS

CN 1-Propanamine, N,N-dimethyl-3-[[10-(phenylmethoxy)dibenzo[b,f]thieno[3,2-d]oxepin-2-yl]methoxy]- (CA INDEX NAME)

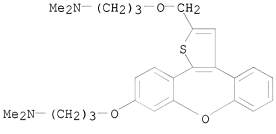


RN 756480-90-7 CAPLUS

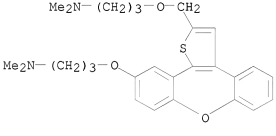
CN 1-Propanamine, N,N-dimethyl-3-[[11-(phenylmethoxy)dibenzo[b,f]thieno[3,2-d]oxepin-2-yl]methoxy]- (CA INDEX NAME)



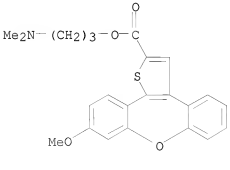
RN 756480-91-8 CAPLUS
CN 1-Propanamine, 3-[[10-[3-(dimethylamino)propoxy]dibenzo[b,f]thieno[2,3-d]oxepin-2-yl]methoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



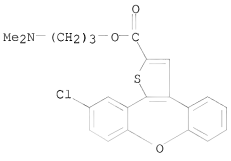
RN 756480-92-9 CAPLUS
CN 1-Propanamine, 3-[[11-[3-(dimethylamino)propoxy]dibenzo[b,f]thieno[2,3-d]oxepin-2-yl]methoxy]-N,N-dimethyl- (9CI) (CA INDEX NAME)



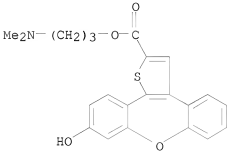
RN 756480-94-1 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxylic acid, 10-methoxy-, 3-(dimethylamino)propyl ester (CA INDEX NAME)



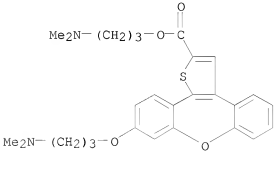
RN 756480-96-3 CAPLUS
CN Dibenzo[b,f]thieno[3,2-d]oxepin-2-carboxylic acid, 11-chloro-, 3-(dimethylamino)propyl ester (CA INDEX NAME)



RN 756480-97-4 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxylic acid, 10-hydroxy-, 3-(dimethylamino)propyl ester (CA INDEX NAME)



RN 756481-07-9 CAPLUS
CN Dibenzo[b,f]thieno[2,3-d]oxepin-2-carboxylic acid, 10-[3-(dimethylamino)propoxy]-, 3-(dimethylamino)propyl ester (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:818427 CAPLUS
DOCUMENT NUMBER: 139:323507
TITLE: Preparation of 1- or 3-thienonaphthazulenes as

inhibitors of tumor necrosis factor production

INVENTOR(S): Mercep, Mladen; Mesic, Milan; Pesic, Dijana; Ozimec, Ivana; Trojko, Rudolf

PATENT ASSIGNEE(S): Pliva D.D., Croatia

SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

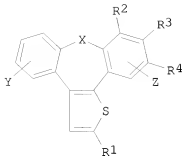
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003084961	A1	20031016	WO 2003-HR14	20030409
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
HR 2002000303	B1	20070531	HR 2002-303	20020410
CA 2481850	A1	20031016	CA 2003-2481850	20030409
AU 2003259958	A1	20031020	AU 2003-259958	20030409
EP 1492795	A1	20050105	EP 2003-745847	20030409
EP 1492795	B1	20051116		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003009097	A	20050209	BR 2003-9097	20030409
CN 1649876	A	20050803	CN 2003-809957	20030409
JP 2005526827	T	20050908	JP 2003-582158	20030409
AT 310005	T	20051215	AT 2003-745847	20030409
NZ 535622	A	20060331	NZ 2003-535622	20030409
ES 2253694	T3	20060601	ES 2003-745847	20030409
RU 2318827	C2	20080310	RU 2004-132866	20030409
ZA 2004008059	A	20051006	ZA 2004-8059	20041006
MX 2004PA09872	A	20050816	MX 2004-PA9872	20041008
US 7262309	B2	20070828	US 2004-963979	20041012
US 20050130964	A1	20050616		
NO 2004004508	A	20041109	NO 2004-4508	20041021
IN 2004CN02522	A	20070921	IN 2004-CN2522	20041109
US 20050137249	A1	20050623	US 2005-510867	20050223

PRIORITY APPLN. INFO.: HR 2002-303 A 20020410
WO 2003-HR14 W 20030409

OTHER SOURCE(S): MARPAT 139:323507

GI



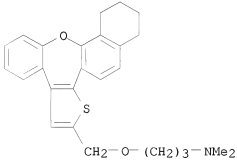
I

AB Thienonaphthazulenes I [X = CH2, O, S, S(O), SO2, NH, protected NH; Y, Z = halogen, alkyl, alkenyl, alkynyl, CF3, haloalkyl, OH, alkoxy, F3CO, acyl, (un)substituted amino, aminoalkyl, SH, alkylthio, alkylsulfinyl, alkylsulfonyl, CO2H, alkoxycarbonyl, NO2; R1 = halogen, (un)substituted alkyl, alkenyl, alkynyl, aryl, heteroaryl, heterocyclic, OH, SH, CO2H, acyl, CONH2, alkylsulfonyl, alkylsulfinyl, NO2; R2R3, R3R4 = (un)substituted CH:CHCH:CH, (CH2)4] were prepared for use as antiinflammatory agents, especially as inhibitors of TNF-α production and interleukin-1 production, as well as analgesics (no data). Thus, I [X = O, Y, Z, R4 = H, R1 = CH2OCH2CH2NMe2, R2R3 = CH:CHCH:CH] was prepared from 2-(2-naphthyloxy)phenylacetic acid, HSCH2CO2Et, and Me2NCH2CH2Cl.HCl.

IT 613671-38-8P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 1- or 3-thienonaphthazulenes as inhibitors of tumor necrosis factor production)

RN 613671-38-8 CAPLUS

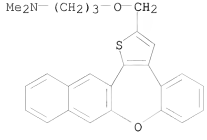
CN 1-Propanamine, N,N-dimethyl-3-[(1,2,3,4-tetrahydrobenzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-yl)methoxy]- (CA INDEX NAME)



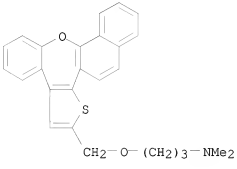
IT 613671-29-7P 613671-35-5P 613671-36-6P
613671-42-4P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1- or 3-thienonaphthazulenes as inhibitors of tumor necrosis factor production)

RN 613671-29-7 CAPLUS

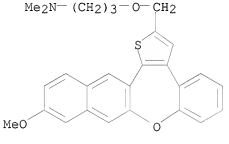
CN 1-Propanamine, 3-(benzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)



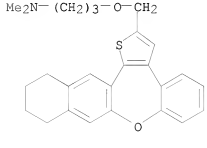
RN 613671-35-5 CAPLUS
CN 1-Propanamine, 3-(benzo[b]naphtho[2,1-f]thieno[3,2-d]oxepin-8-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)



RN 613671-36-6 CAPLUS
CN 1-Propanamine, 3-[(11-methoxybenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



RN 613671-42-4 CAPLUS
CN 1-Propanamine, N,N-dimethyl-3-[(10,11,12,13-tetrahydrobenzo[b]naphtho[2,3-f]thieno[3,2-d]oxepin-2-yl)methoxy]- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:851165 CAPLUS
DOCUMENT NUMBER: 136:5998
TITLE: Preparation of thienodibenzoazulene compounds as inhibitors of tumor necrosis factor and interleukin production
INVENTOR(S): Mercep, Mladen; Mesic, Milan; Pesic, Dijana; Zupanovic, Zeljko; Hrvacic, Boska
PATENT ASSIGNEE(S): Pliva, Farmaceutska Industrija, Dionicko Drustvo, Croatia
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087890	A1	20011122	WO 2001-HR27	20010516
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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HR 2000000310	A1	20020228	HR 2000-310	20000517
CA 2409090	A1	20011122	CA 2001-2409090	20010516
AU 2001056560	A	20011126	AU 2001-56560	20010516
EP 1284977	A1	20030226	EP 2001-929882	20010516
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001011202	A	20030401	BR 2001-11202	20010516
HU 2003002295	A2	20031028	HU 2003-2295	20010516
HU 2003002295	A3	20070328		
JP 2003533528	T	20031111	JP 2001-584284	20010516
EE 200200636	A	20040415	EE 2002-636	20010516
CN 1194976	C	20050330	CN 2001-811589	20010516
NZ 522553	A	20050429	NZ 2001-522553	20010516
AU 2001256560	B2	20051006	AU 2001-256560	20010516
ZA 2002009180	A	20031112	ZA 2002-9180	20021112
NO 2002005510	A	20030114	NO 2002-5510	20021115
MX 2002PA11269	A	20030606	MX 2002-PA11269	20021115
US 20030153750	A1	20030814	US 2002-298217	20021118
US 6897211	B2	20050524		
KR 823064	B1	20080418	KR 2002-715567	20021118
IN 2002CN02041	A	20050225	IN 2002-CN2041	20021211
BG 107399	A	20030930	BG 2002-107399	20021217
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US 20050171091	A1	20050804	US 2005-90743	20050325

PRIORITY APPLN. INFO.:
HR 2000-310 A 20000517
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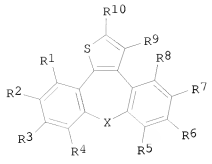
OTHER SOURCE(S): CASREACT 136:5998; MARPAT 136:5998
GI



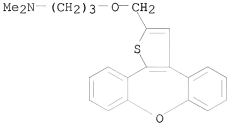
I

AB The title compds. [I; X = CH2, a heteroatom such as O, S, S(O), S(O)2 or NR13(wherein R13 = H, C1-6 alkyl, C1-6 alkylcarbonyl, arylcarbonyl, C1-6 alkylsulfonyl, arylsulfonyl); R1, R2, R3, R4, R5, R6, R7, R5, R9 = H, halogens (fluorine, chlorine or bromine), C1-7 alkyl, alkenyl, aryl, heteroaryl; or they can represent different groups : halomethyl, hydroxy, C1-7 alkoxy or aryloxy, C1-7 alkylthio or arylthio, C1-7 alkylsulfonyl, cyano, amino, mono- and di(C1-7 substituted) amines, derivs. of carboxylic group (C1-C7 carboxylic acids and their anhydrides, C1-7 unsubstituted or mono- or disubstituted amides, C1-7 alkyl or aryl esters), C1-7 derivs. of carbonyl group (C1-7 alkyl or arylcarbonyls); R10 = C2-15 alkyl, C2-15 alkenyl, C2-15 alkynyl, aryl or heteroaryl, C1-15 haloalkyl, C1-15 hydroxyalkyl, C1-15 alkoxy, C1-15 alkylthio, C3-15 alkylcarbonyl, C2-15 alkylcarboxylic acid, C2-15 alkyl ester, C1-15 alkylsulfonyl, C1-15 alkylarylsulfonyl, arylsulfonyl, C1-15 alkylamines represented by the general formula -(CH2)n-A (wherein n means 1-15, and one or more methylene groups that can be substituted with an oxygen or sulfur atom, and A represents a five- or six-membered, saturated or unsatd. ring with one, two or three heteroatoms, or -NR11R12; wherein R11 and R12 independently from each other represent hydrogen, C1-7 alkyl, alkenyl, alkynyl, aryl or heteroaryl, or a heterocycle with 1-3 heteroatoms)] are prepared These compds. I are inhibitors of the production of cytokines or inflammation mediators, e.g. tumor necrosis factor alpha (TNF-α) and interleukin 1 (IL-1), and useful for the treatment or prophylaxis of any pathol. conditions or diseases induced by excessive unregulated production of cytokines or inflammation mediators. They also demonstrate an analgetic action and can be used to relieve pain and thereby useful as anti-inflammatory agents, inhibitors of TNF-α and IL-1 secretion, or analgesics. Thus, 0.1 g benzyltriethylammonium chloride and a toluene solution of 0.28 g 2-(hydroxymethyl)-8-oxa-1-thia-dibenzo[e,h]azulene were added to a solution of 2.2 g 3-dimethylaminopropyl chloride hydrochloride in 5 mL 50% aqueous NaOH and the resulting mixture was refluxed for 4 h with vigorous stirring to give dimethyl-[3-(8-oxa-1-thia-dibenzo[e,h]azulen-2-ylmethoxy)propyl]amine (II). II.HCl and 3 other I demonstrated activity in at least two of investigated biol. tests such as TNF-α and IL-1 secretion in mononuclear cells of human peripheral blood or mouse peritoneal macrophages in vitro, LPS-induced excessive secretion of TNF-α or IL-1 in mice, writhing test for analgesic activity in mice, and LPS-induced shock in mice (no detailed data given).

IT 374799-32-3P, Dimethyl-[3-[8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]propyl]amine hydrochloride 374799-34-5P, Dimethyl-[3-[8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]propyl]amine 374799-56-1P, [3-[9-Chloro-8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]propyl]dimethylamine 374799-68-5P, [3-[11-Chloro-8-oxa-1-thiadibenzo[e,h]azulen-2-ylmethoxy]propyl]dimethylamine 374799-79-8P 374799-81-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

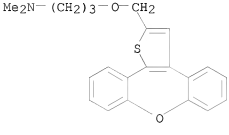
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of thienodibenzoazulene compds. as tumor necrosis factor and interleukin production inhibitors, antiinflammatory agents, and analgesics)

RN 374799-32-3 CAPLUS
CN 1-Propanamine, 3-(dibenzo[b,f]thieno[2,3-d]oxepin-2-ylmethoxy)-N,N-dimethyl-, hydrochloride (1:1) (CA INDEX NAME)

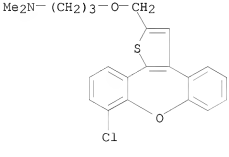


● HCl

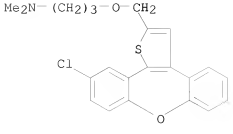
RN 374799-34-5 CAPLUS
CN 1-Propanamine, 3-(dibenzo[b,f]thieno[2,3-d]oxepin-2-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)



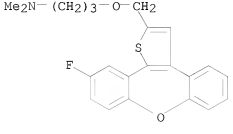
RN 374799-56-1 CAPLUS
CN 1-Propanamine, 3-[(9-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



RN 374799-68-5 CAPLUS
CN 1-Propanamine, 3-[(11-chlorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)

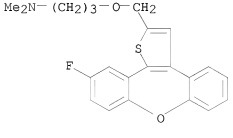


RN 374799-79-8 CAPLUS
CN 1-Propanamine, 3-[(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

RN 374799-81-2 CAPLUS
CN 1-Propanamine, 3-[(11-fluorodibenzo[b,f]thieno[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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